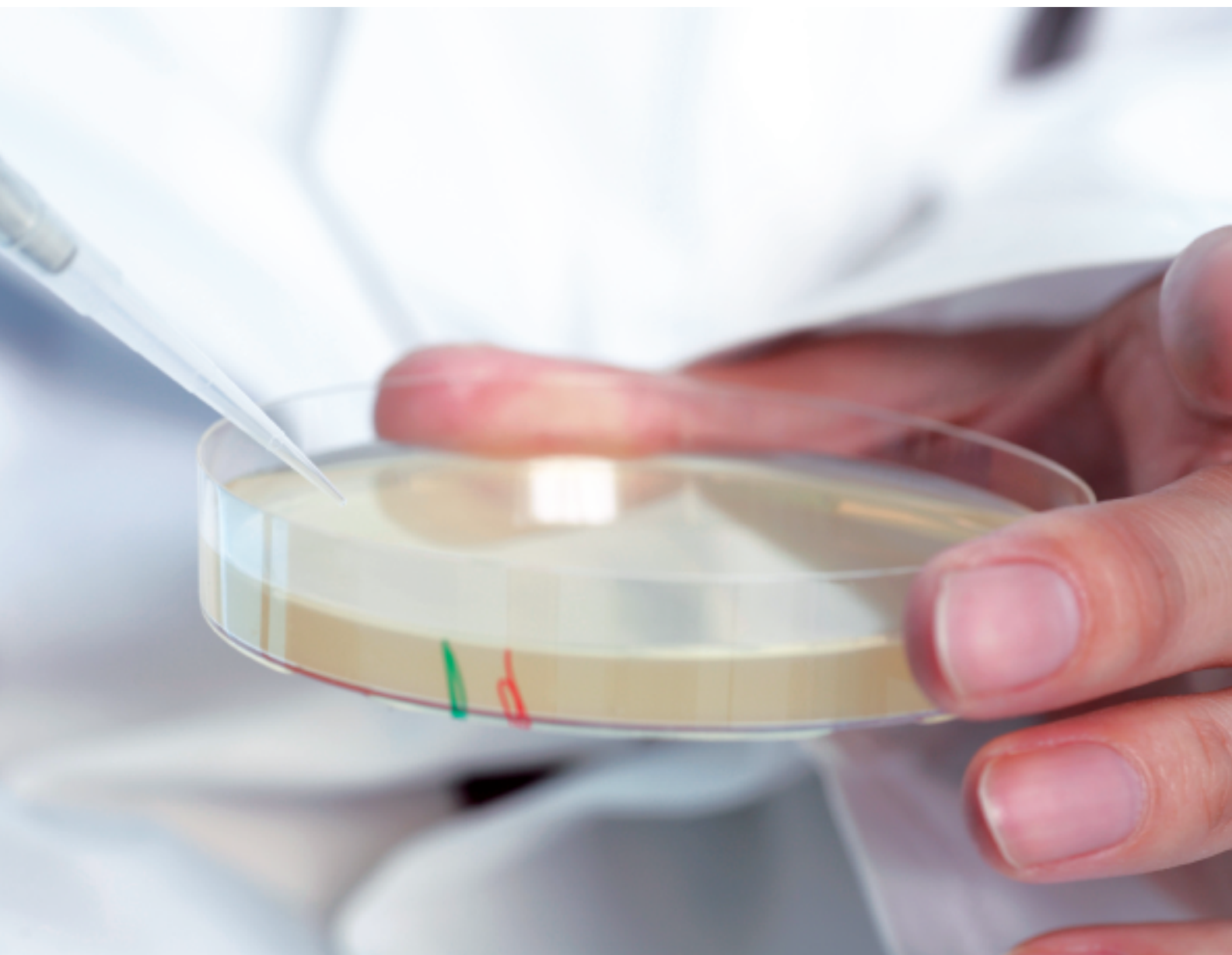




Federal Ministry
of Health

Federal Ministry
of Food, Agriculture and
Consumer Protection

Federal Ministry
of Education
and Research



DART

German Antimicrobial Resistance Strategy

www.bmg.bund.de

**Federal Ministry of Health
D-11055 Berlin, Germany**

**In collaboration with:
Federal Ministry of Food, Agriculture and Consumer Protection
Federal Ministry of Education and Research**

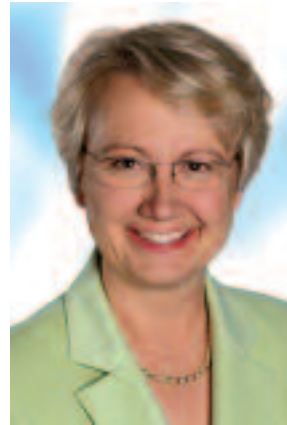
Berlin, November 2008



Ulla Schmidt,
Federal Minister
of Health



Ilse Aigner,
Federal Minister of Food,
Agriculture and Consumer
Protection



Dr. Anette Schavan,
Federal Minister of Education
and Research

Jointly fighting antimicrobial resistance

For a long time, it was commonly believed that the discovery of penicillin and the use of antibiotics meant that bacterial infections had been conquered for all time. In recent years, however, we have been observing an increase in antimicrobially resistant infective agents in both human and veterinary medicine. This makes it increasingly difficult to successfully treat infections.

DART, the German Antimicrobial Resistance Strategy, presents a concept for containing antimicrobial resistance. **DART** defines the targets and actions on which Germany will be concentrating in its international and national efforts to combat antimicrobial resistance in the next five years.

We will take systematic steps to counteract the principal causes of resistance development: the inappropriate use of antibiotics and inconsistent implementation of recommendations on the prevention of infections. In addition, we will be expanding surveillance systems for antimicrobial resistance and antibiotic consumption, intensifying prevention and control measures, promoting regional, national and international cooperation projects, and strengthening science and research in this field.

DART is designed to contain antimicrobial resistance in Germany. We therefore request the cooperation of all the responsible players in this field in order to implement the strategy.

Ulla Schmidt Ilse Aigner Anette Schavan

In cooperation with:

- Aktionsbündnis Patientensicherheit e. V.
(German Coalition for Patient Safety)
- Arzneimittelkommission der deutschen Ärzteschaft (AkdÄ)
(Drug Commission of the German Medical Association)
- Ärztekammer Nordrhein
(North Rhine Chamber of Physicians)
- Bayerisches Staatsministerium für Umwelt, Gesundheit und Verbraucherschutz
(Bavarian State Ministry for the Environment, Health and Consumer Protection)
- Behörde für Soziales, Familie, Gesundheit und Verbraucherschutz, Hamburg
(Agency for Social Affairs, Family, Health and Consumer Protection, Hamburg)
- Bundesamt für Verbraucherschutz und Lebensmittelsicherheit (BVL)
(Federal Office for Consumer Protection and Food Safety)
- Bundesärztekammer (BÄK)
(German Medical Association)
- Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM)
(Federal Institute for Drugs and Medical Devices)
- Bundesinstitut für Risikobewertung (BfR)
(Federal Institute for Risk Assessment)
- Bundestierärztekammer (BTK)
(Federal Veterinary Association)
- Bundesverband der Arzneimittelhersteller e. V. (BAH)
(Federal Association of Pharmaceutical Manufacturers)
- Bundesverband der Pharmazeutischen Industrie e. V. (BPI)
(Federal Association of the Pharmaceutical Industry)
- Bundesverband Deutscher Krankenhausapotheker (ADKA) e. V.
(German Society of Hospital Pharmacists)
- Bundesverband praktizierender Tierärzte e. V. (bpt)
(Federal Association of Practising Veterinaries)
- Bundeszentrale für gesundheitliche Aufklärung (BZgA)
(Federal Centre for Health Education)
- Deutsche Gesellschaft für Infektiologie e. V. (dgi)
(German Society for Infectious Diseases)
- Deutsche Krankenhausgesellschaft (DKG)
(German Hospital Federation)
- Deutsches Institut für Medizinische Dokumentation und Information (DIMDI)
(German Institute of Medical Documentation and Information)
- Friedrich-Loeffler-Institut (FLI)
(Friedrich Loeffler Institute)
- GKV-Spitzenverband der Krankenkassen
(Head Association of the Statutory Health Insurance Scheme)
- Institut für Medizinische Mikrobiologie und Infektionsepidemiologie der Universität Leipzig
(Institute for Medical Microbiology and Infection Epidemiology of the University of Leipzig)
- Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (IQWiG)
(Institute for Quality and Efficiency in Health Care)
- Kassenärztliche Bundesvereinigung (KBV)
(National Association of SHI-Accredited Physicians)
- Kommission für Krankenhaushygiene und Infektionsprävention (KRINKO)
(Commission on Hospital Hygiene and Infectious Disease Prevention)

- Landesärztekammer Brandenburg
(Brandenburg State Chamber of Physicians)
- Landesinstitut für Gesundheit und Arbeit des Landes Nordrhein-Westfalen
(State Institute for Health and Labour of North Rhine-Westphalia)
- Ministerium für Arbeit und Soziales, Baden-Württemberg
(Ministry of Labour and Social Affairs, Baden-Württemberg)
- Ministerium für Arbeit, Gesundheit und Soziales des Landes Nordrhein-Westfalen
(Ministry of Labour, Health and Social Affairs of North Rhine-Westphalia)
- Ministerium für Soziales und Gesundheit, Mecklenburg-Vorpommern
(Ministry of Social Affairs and Health, Mecklenburg-Western Pomerania)
- Ministerium für Soziales, Gesundheit, Familie, Jugend und Senioren des Landes Schleswig-Holstein
(Ministry of Social Affairs, Health, Family, Youth and Senior Citizens of Schleswig-Holstein)
- Nationales Referenzzentrum für Streptokokken
(National Reference Centre for Streptococci)
- Nationales Referenzzentrum für Surveillance von nosokomialen Infektionen
(National Reference Centre for Surveillance of Nosocomial Infections)
- Niedersächsisches Ministerium für Soziales, Frauen, Familie und Gesundheit
(Ministry for Social Affairs, Women, Family and Health of Lower Saxony)
- Paul-Ehrlich-Gesellschaft für Chemotherapie (PEG)
(Paul Ehrlich Society for Chemotherapy)
- Paul-Ehrlich-Institut (PEI)
(Paul Ehrlich Institute)
- Robert Koch-Institut (RKI)
(Robert Koch Institute)
- Saarländisches Ministerium für Justiz, Arbeit, Gesundheit und Soziales
(Ministry of Justice, Labour, Health and Social Affairs of the Saarland)
- Senat für Arbeit, Frauen, Gesundheit, Jugend und Soziales, Bremen
(Senate for Labour, Women, Health, Youth and Social Affairs, Bremen)
- Senatsverwaltung für Gesundheit, Umwelt und Verbraucherschutz, Berlin
(Senate Administration for Health, Environment and Consumer Protection, Berlin)
- Verband der Diagnostica-Industrie e. V. (VDGH)
(Diagnostics Industry Association)
- Verband Forschender Arzneimittelhersteller e. V. (VFA)
(Association of Research-Based Pharmaceutical Companies)
- World Health Organization (WHO)
- Wissenschaftliches Institut der AOK (WIdO)
(Scientific Institute of the Local Health Care Funds)
- Wissenschaftszentrum Berlin für Sozialforschung (WZB)
(Social Science Research Center Berlin)
- Zentrum für Klinische Infektiologie (IF), Freiburg
(Centre for Infectious Diseases, Freiburg)

Contents

Foreword	1
List of abbreviations	8
1 Summary	10
1.1 Human medicine	11
1.2 Veterinary medicine	12
2 Principles of antimicrobial resistance	13
2.1 What is antimicrobial resistance?	13
2.2 Causes of resistance development	14
2.3 What is the problem with antimicrobial resistance?	15
3 International situation in the field of antimicrobial resistance	16
4 German situation in the field of antimicrobial resistance	18
4.1 Human medicine	18
4.1.1 Antimicrobial resistance data	18
4.1.2 Antibiotic consumption data	19
4.1.3 Recommendations and guidelines for preventing and controlling antimicrobial resistance	20
4.1.4 Basic training, specialist training and continuing education of medical occupational groups, pharmacists and natural scientists	21
4.1.5 Further supportive measures for preventing and controlling antimicrobial resistance	21
4.1.6 Research	21
4.1.6.1 Research activities on antimicrobial resistance in the portfolio of the BMG	21
4.1.6.2 Need for research and development	22
4.1.7 Necessity of a national, interdisciplinary strategy	23
4.2 Veterinary medicine	24
4.2.1 Importance of antimicrobial resistance for the field of animal husbandry, the food chain and veterinary activity	24
4.2.2 Aims of the Antimicrobial Resistance Strategy for the field of animal husbandry, the food chain and veterinary activity	24
4.3 Environment	25

5	DART in the field of human medicine	26
5.1	Principal goal of the strategy	26
5.2	National goals	26
	Component I: Surveillance systems for antimicrobial resistance and antibiotic consumption	27
	Goal 1: Strengthening of the surveillance systems for antimicrobial resistance and antibiotic consumption	27
	Sub-goal 1.1: Strengthening of the surveillance systems for recording and assessing antimicrobial resistance	27
	Sub-goal 1.2: Strengthening of the monitoring systems for recording and assessing antibiotic consumption	28
	Goal 2: Systematic feedback of data on antimicrobial resistance and antibiotic consumption	28
	Sub-goal 2.1: Establishment of a feedback system	28
	Sub-goal 2.2: Expansion of the system of National Reference Centres	29
	Sub-goal 2.3: Establishment of an early-warning system	29
	Sub-goal 2.4: Introduction of quality indicators in the field of antimicrobial resistance	29
	Component II: Prevention and control measures for reducing antimicrobial resistance	30
	Goal 3: Promotion of the application of guidelines	30
	Sub-goal 3.1: Development of guidelines	30
	Sub-goal 3.2: Promotion of structures for applying guidelines and recommendations	31
	Goal 4: Safeguarding diagnosis	31
	Goal 5: Promotion of the basic training, specialist training and continuing education of medical occupational groups, pharmacists and natural scientists	32
	Component III: Cooperation and coordination	33
	Goal 6: National cooperation	33
	Sub-goal 6.1: Cooperation at the regional level	33
	Sub-goal 6.2: Cooperation at the Federal Government level	34
	Sub-goal 6.3: Coordination of activities at the national level	34
	Goal 7: International cooperation	35
	Component IV: Research and evaluation	35
	Goal 8: Promotion of evaluation measures in human medicine	35
	Goal 9: Promotion of knowledge transfer in the field of antimicrobial resistance	36
	Goal 10: Networking and strengthening of science in the field of antimicrobial resistance	37
6	DART in the field of animal husbandry, the food chain and veterinary activity	38
6.1	Existing measures for minimising antimicrobial resistance	38
6.1.1	Measures in Germany	39
6.1.1.1	Legal bases	39
6.1.1.2	Monitoring	40
6.1.1.2.1	National Reference Laboratory for Antimicrobial Resistance	40
6.1.1.2.2	Monitoring and testing of pathogens of importance for human health	40
6.1.1.2.3	Monitoring of resistance in zoonotic agents	41
6.1.1.2.4	Active substance-specific monitoring studies	41

6.1.1.3	Registration and pharmacovigilance for antibiotics for veterinary medicine	42
6.1.1.3.1	Registration requirements for antibiotics for veterinary medicine	42
6.1.1.3.2	Pharmacovigilance	42
6.1.1.4	Regulations on the sale of antibiotics for systemic use	42
6.1.1.4.1	Recording of the quantities of antibiotics sold	43
6.1.1.4.2	Recording of the quantities of antibiotics used	43
6.1.1.5	Antibiotic Guidelines	44
6.1.1.6	Use of antibiotically active substances in food production	44
6.1.1.7	Use of streptomycin against fire blight in pomaceous fruit	45
6.1.1.7.1	First strategy from 2003	45
6.1.1.7.2	Orderly termination of the use of antibiotics	45
6.1.1.8	Sensitisation and education	46
6.1.1.8.1	Risk communication	46
6.1.1.8.2	Scientific expert events and publications	46
6.1.1.9	Training and continuing education	47
6.1.2	International measures	47
6.1.2.1	Measures at the European level	47
6.1.2.1.1	Activities of the European Food Safety Authority	47
6.1.2.1.2	Studies on antimicrobial resistance	48
6.1.2.1.3	Harmonisation of measures	48
6.1.2.2	Supranational measures	48
6.1.2.2.1	Specifications of the World Organisation for Animal Health	48
6.1.2.2.2	Specifications of the WHO/FAO (Codex Alimentarius)	49
6.2	Future national measures for minimising antimicrobial resistances	49
6.2.1	Recording of the quantities of antibiotics sold	49
6.2.2	Recording of the quantities of antibiotics used	50
6.2.3	Expansion of resistance monitoring	50
6.2.4	Standardisation of resistance determination	50
6.2.5	Monitoring of antibiotic efficacy	51
6.2.6	Annual antimicrobial resistance report	51
6.2.7	Antibiotic guidelines	51
6.3	Research into antimicrobial resistance and the avoidance of antimicrobial resistance	52
6.3.1	Antimicrobial resistance research activities in the portfolio of the BMELV	52
6.3.2	Research and development requirement	52
6.3.2.1	Antimicrobial resistance characteristics and mechanisms	53
6.3.2.2	Promotion of the development of alternatives to the use of antibiotics	53
6.3.2.3	Promotion of research into the optimisation of antibiotic and vaccine use, and into the optimisation of monitoring	54

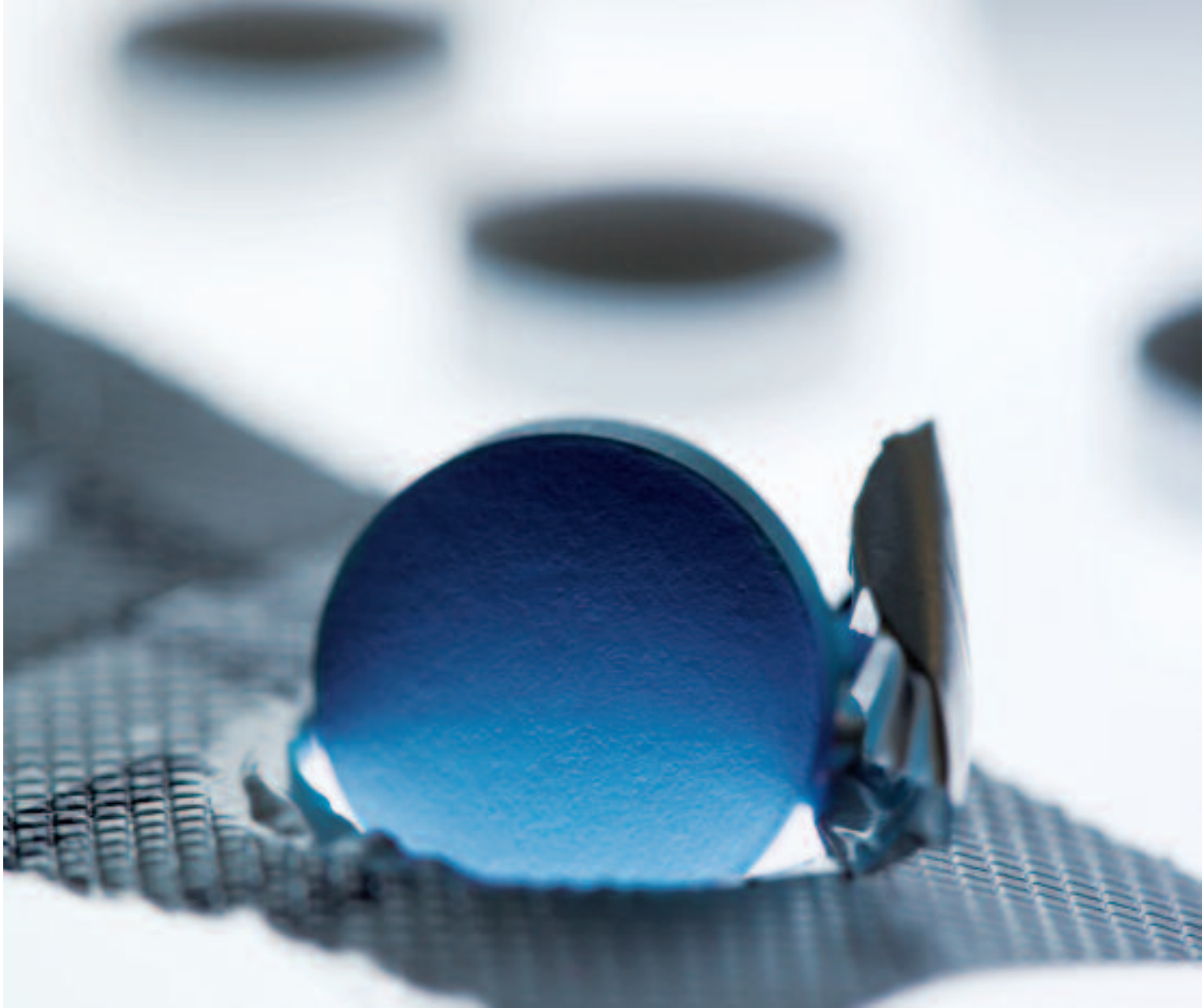
Appendix 55

1.1	Overview of the planned structure	56
1.2	Overview of the actions planned in the field of human medicine	57
1.3	Projects and activities in Germany in the field of antimicrobial resistance in human medicine	60
1.3.1	Surveillance of antimicrobial resistance	60
1.3.2	Antibiotic consumption	62
1.3.3	Prevention and control of antimicrobial resistance	64
1.3.3.1	Recommendations	64
1.3.3.1.1	Diagnostics	64

1.3.3.1.2	Therapy	65
1.3.3.1.3	Hygiene	65
1.3.3.1.4	Quality assurance	65
1.3.3.2	Basic training, specialist training and continuing education of medical occupational groups	66
1.3.3.3	Networks	67
1.3.3.4	Public relations campaigns	68
1.4	Antimicrobial resistance in an international context	69
1.4.1	European Commission	69
1.4.2	European Academy Science Advisory Council (EASAC)	69
1.4.3	European Centre for Disease Prevention and Control (ECDC)	69
1.4.4	World Health Organization (WHO)	70
1.5	Players in the field of antimicrobial resistance	70
	References	85

ABDA	Bundesvereinigung Deutscher Apothekerverbände (Federal Union of German Associations of Pharmacists)	BZÄK	Bundeszahnärztekammer (German Dental Association)
ABS	Antibiotic Stewardship	BzGA	Bundeszentrale für gesundheitliche Aufklärung (Federal Centre for Health Education)
ADKA	Bundesverband Deutscher Krankenhausapotheker e. V. (German Society of Hospital Pharmacists)	CAPNETZ	Kompetenznetz Ambulant Erworbene Pneumonien (Community-Acquired Pneumonia Competence Network)
AGI	Arbeitsgruppe Infektionsschutz (Infection Protection Working Group)	CDAD	Clostridium difficile-Associated Diarrhoea
AIDS	Acquired Immune Deficiency Syndrome	CLSI	Clinical and Laboratory Standard Institute
AKdÄ	Arzneimittelkommission der Deutschen Ärzteschaft (Drug Commission of the German Medical Association)	CRL	Community Reference Laboratory
AMG	Arzneimittelgesetz (German Drug Law)	CVMP	Committee for Veterinary Medicinal Products
AOK	Allgemeine Ortskrankenkasse (Local Health Insurance Fund)	DART	Deutsche Antibiotika-Resistenzstrategie (German Antimicrobial Resistance Strategy)
APS	Aktionsbündnis Patientensicherheit e. V. (German Coalition for Patient Safety)	DBV	Deutscher Bauernverband (German Farmers Association)
ARMIN	Antibiotika Resistenz Monitoring in Niedersachsen (Antimicrobial Resistance Monitoring in Lower Saxony)	DEGAM	Deutsche Gesellschaft für Allgemeinmedizin und Familienmedizin (German Society for General and Family Medicine)
ARS	Antimicrobial Resistance Surveillance	DFG	Deutsche Forschungsgemeinschaft (German Research Foundation)
AWMF	Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften e. V. (Association of the Scientific Medical Societies in Germany)	DGAI	Deutsche Gesellschaft für Anästhesiologie und Intensivmedizin e. V. (German Society for Anaesthesiology and Intensive Care Medicine)
ÄZQ	Ärztliches Zentrum für Qualität in der Medizin (Agency for Quality in Medicine)	DGCH	Deutsche Gesellschaft für Chirurgie (German Society for Surgery)
BAH	Bundesverband der Arzneimittel-Hersteller e. V. (Federal Association of Pharmaceutical Manufacturers)	DGHM	Deutsche Gesellschaft für Hygiene und Mikrobiologie (German Society for Hygiene and Microbiology)
BÄK	Bundesärztekammer (German Medical Association)	DGI	Deutsche Gesellschaft für Infektiologie (German Society for Infectious Diseases)
BÄMI	Bundesverband der Ärzte für Mikrobiologie und Infektions-epidemiologie (Federal Association of Doctors for Microbiology and Infection Epidemiology)	DGIM	Deutsche Gesellschaft für Innere Medizin (German Society for Internal Medicine)
BDA	Berufsverband Deutscher Anästhesisten e. V. (Association of German Anaesthetists)	DGKH	Deutsche Gesellschaft für Krankenhaushygiene (German Society for Hospital Hygiene)
BDH	Berufsverband Deutscher Hygieniker (German Association of Hygiene Specialists)	DGP	Deutsche Gesellschaft für Pneumologie e. V. (German Society for Pneumology)
BDI	Berufsverband Deutscher Internisten (German Association of Internists)	DGPI	Fachgesellschaft für Pädiatrische Infektiologie (Society for Paediatric Infectious Diseases)
BfArM	Bundesinstitut für Arzneimittel und Medizinprodukte (Federal Institute for Drugs and Medical Devices)	DGU	Deutsche Gesellschaft für Unfallchirurgie (German Society for Trauma and Emergency Surgery)
BfR	Bundesinstitut für Risikobewertung (Federal Institute for Risk Assessment)	DIMDI	Deutsches Institut für Medizinische Dokumentation und Information (German Institute of Medical Documentation and Information)
BfT	Bundesverband für Tiergesundheit (Federal Association for Animal Health)	DIN	Deutsches Institut für Normung (German Institute for Standardization)
BMBF	Bundesministerium für Bildung und Forschung (Federal Ministry of Education and Research)	DKG	Deutsche Krankenhausgesellschaft (German Hospital Federation)
BMELV	Bundesministerium für Ernährung, Landwirtschaft und Verbraucherschutz (Federal Ministry of Food, Agriculture and Consumer Protection)	DLR	Deutsches Zentrum für Luft- und Raumfahrt (German Aerospace Centre)
BMG	Bundesministerium für Gesundheit (Federal Ministry of Health)	DPR	Deutscher Pflegerat e. V. (German Nursing Council)
BMU	Bundesministerium für Umwelt, Naturschutz und Reaktorsicherheit (Federal Ministry for the Environment, Nature Conservation and Nuclear Safety)	DVG	Deutsche Veterinärmedizinische Gesellschaft (German Society for Veterinary Medicine)
BMWi	Bundesministerium für Wirtschaft und Technologie (Federal Ministry of Economics and Technology)	E. coli	Escherichia coli
BPT	Bundesverband praktizierender Tierärzte (Federal Association of Practising Veterinarians)	EARSS	European Antimicrobial Resistance Surveillance System
BQS	Bundesgeschäftsstelle Qualitätssicherung (German National Institute for Quality Measurement in Health Care)	EASAC	European Academy Science Advisory Council
BTK	Bundestierärztekammer (German Veterinary Association)	EC	European Community
BVL	Bundesamt für Verbraucherschutz und Lebensmittelsicherheit (Federal Office for Consumer Protection and Food Safety)	ECDC	European Centre for Disease Prevention and Control
BVÖGD	Bundesverband der Ärzte des öffentlichen Gesundheitswesens (Federal Association of Public Health Service Physicians)	EFSA	European Food Safety Authority
		EMA	European Medicines Agency
		ESAC	European Surveillance of Antimicrobial Consumption
		ESCMID	European Society for Clinical Microbiology and Infectious Diseases
		EU	European Union
		EU COM	European Commission
		EUCAST	European Committee on Antimicrobial Susceptibility Testing

FAL	Bundesforschungsanstalt für Landwirtschaft (Federal Agricultural Research Centre)	PSUR	Periodic Safety Update Report
FAO	Food and Agriculture Organization of the United Nations	PT-DLR	Projekträger im Deutschen Zentrum für Luft- und Raumfahrt (Project Management Agency of the German Aerospace Centre)
FLI	Friedrich Loeffler Institute		
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)	RKI	Robert Koch Institute
GENARS	German Network for Antimicrobial Resistance Surveillance	SAGAM	Scientific Advisory Group on Antimicrobials
GFB	Gemeinschaft fachärztlicher Berufsverbände (Federation of Professional Associations of Medical Specialists)	SARI	Surveillance of Antimicrobial Use and Antimicrobial Resistance in Intensive Care Units
GKV	Gesetzliche Krankenversicherung (Statutory Health Insurance – SHI)	S. aureus	Staphylococcus aureus
GMK	Gesundheitsministerkonferenz der Länder (Conference of Ministers Responsible for Health)	SCF	Scientific Committee on Food
GWB	Gemeinsamer Wissenschaftlicher Beirat (Joint Scientific Advisory Board)	SHI	Statutory Health Insurance
HIV	Human Immunodeficiency Virus	TÄHAV	Verordnung über tierärztliche Hausapotheken (Veterinary House Dispensary Ordinance)
IF	Infektiologie Freiburg (Freiburg Centre for Infectious Diseases)	VAAM	Vereinigung für Allgemeine und Angewandte Mikrobiologie (Association for General and Applied Microbiology)
IfSG	Infektionsschutzgesetz (Protection Against Infection Act)	VAH	Verbund für Angewandte Hygiene (Association for Applied Hygiene)
INSTAND	Gesellschaft zur Förderung der Qualitätssicherung in medizinischen Laboratorien e. V. (Society for Promotion of Quality Assurance in Medical Laboratories)	VDGH	Verband der Diagnostica Industrie e. V. (Diagnostics Industry Association)
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)	VFA	Verband Forschender Arzneimittelhersteller e. V. (Association of Research-Based Pharmaceutical Companies)
KBV	Kassenärztliche Bundesvereinigung (National Association of SHI-Accredited Physicians)	VHD	Verein der Hygiene-Fachkräfte der Bundesrepublik Deutschland e. V. (Association of Hygiene Professionals in the Federal Republic of Germany)
KIGGS	Kinder- und Jugendgesundheitssurvey (German Health Survey for Children and Adolescents)	VLK	Verband der Leitenden Krankenhausärzte Deutschlands e. V. (Association of Senior Hospital Physicians in Germany)
KISS	Krankenhaus-Infektions-Surveillance-System (Hospital Infection Surveillance System)	VRE	Vancomycin-Resistant Enterococci
KRINKO	Kommission für Krankenhaushygiene und Infektionsprävention (Commission on Hospital Hygiene and Infectious Disease Prevention)	WGL	Wissenschaftsgemeinschaft Gottfried Wilhelm Leibniz (Gottfried Wilhelm Leibniz Scientific Association)
LÄK	Landesärztekammer (State Chamber of Physicians)	WHA	World Health Assembly
LAVES	Landesamt für Verbraucherschutz und Lebensmittelsicherheit, Niedersachsen (State Office for Consumer Protection and Food Safety, Lower Saxony)	WHO	World Health Organization
LFGB	Lebensmittel- und Futtermittelgesetzbuch (Food and Feed Code)	WIdO	Wissenschaftliches Institut der Ortskrankenkassen (Scientific Institute of the Local Health Care Funds)
LIGA	Landesinstitut für Gesundheit und Arbeit des Landes Nordrhein-Westfalen (State Institute for Health and Work, North Rhine-Westphalia)	Z.A.R.S.	Zentralstelle für die Auswertung von Resistenzdaten bei systemisch wirkenden Antibiotika (Central Office for the Evaluation of Resistance Data on Systemic Antibiotics)
MABUSE	Medical Antibiotic Use Surveillance and Evaluation		
MIC	Minimum Inhibitory Concentration		
MRSA	Methicillin-Resistant Staphylococcus aureus		
MFT	Medizinischer Fakultätstag (Medical Faculty Association)		
NIP	Nosocomial Infection Prevention		
NRL-AR	National Reference Laboratory for Antimicrobial Resistance		
NRC	National Reference Centre		
ÖGD	Öffentlicher Gesundheitsdienst (Public Health Service)		
OIE	World Organisation for Animal Health		
PEG	Paul-Ehrlich-Gesellschaft für Chemotherapie (Paul Ehrlich Society for Chemotherapy)		
PKV	Verband der privaten Krankenversicherung e. V. (Association of Private Health Insurers)		



1 Summary

Infectious diseases are the most common cause of death worldwide. In Germany, more than 40,000 people died of the consequences of an infection in 2006, over 50 % of them of the consequences of pneumonia. Pneumonia was the seventh most frequent cause of death in Germany in 2006. The number of deaths caused by an infection rose by 14 % in Germany between the years 2002 and 2006. The number of deaths in which an infection is a contributory factor is even higher, since infectious diseases often occur as concomitant illnesses and are thus not recorded as the cause of death.

The treatment of bacterial infectious diseases is becoming increasingly difficult as a result of the growing number of antimicrobially resistant pathogens. For the patients, this often means longer treatment periods, and also additional stress resulting from the fact that the curing of an

infection is either delayed or fails to materialise at all. Since the percentage of resistant pathogens has risen in recent years, and a further increase cannot be ruled out, a targeted approach is needed to reduce antimicrobial resistance and strengthen preventive measures at the local, regional and national level.

The containment of antimicrobial resistance necessitates a comprehensive examination of the problem, since antimicrobial resistance occurs both in the field of human medicine and in veterinary medicine. Consequently, the present Antimicrobial Resistance Strategy was developed in collaboration with responsible stakeholders in the health sector, as well as in the field of animal husbandry, the food chain and veterinary activity. The German Antimicrobial Resistance Strategy, **DART**, contains measures for detecting, preventing and controlling antimicro-

bial re-sistances in Germany. The central goal is to reduce the number and spread of antimicrobial resistances in Germany.

1.1 Human medicine

The requirements were analysed, and the necessary measures for containing antimicrobial resistance determined, by drawing up a systematic compilation and assessment of national activities and a comparison with international programmes for prevention and control of antimicrobial resistance. This served as the basis for elaborating the human-medicine segment of the strategy and for formulating its goals and actions.

To achieve the central goal of reducing the number and spread of antimicrobial resistances, one particular aim is to work towards appropriate use of antibiotics and consistent application of infection hygiene.

At the federal level, the key legal instruments for the surveillance of resistant pathogens, for infection-related hygiene and its monitoring, and for the prevention and control of infections caused by resistant pathogens, are defined in the Protection Against Infection Act (IfSG). The German States ("Länder") have in some cases also issued supplementary regulations. Consistent implementation of the legal targets by the competent enforcement agencies, and by the responsible players in medical institutions, makes an essential contribution to achieving the central goal of the strategy.

On the basis of, and expanding on, this set of legal instruments, the strategy formulates ten goals for reducing the number of spread of antimicrobial resistances. Actions and players are assigned to each goal, and a milestone is assigned to each action. A total of 42 actions are envisaged, involving diverse, interconnected measures to be implemented in the period from 2008 to 2013. The ten goals can be assigned to the following four fields of action:

I. Expanding surveillance systems for antimicrobial resistance and antibiotic consumption

Surveillance systems for collecting and assessing data on antimicrobial resistance and antibiotic consumption are to be strengthened. An appropriate feedback system is to be used to pass back the analysed data to physicians who prescribe antibiotics. The expansion of an early-warning and response system is intended to guarantee early

detection of pathogens displaying new resistances or resistance patterns, and of increasing regional/local accumulations or elevated incidences of certain resistant pathogens. Depending on the problem in question, targeted containment measures can then be initiated via the response system.

II. Strengthening of prevention and control measures for reducing antimicrobial resistance

To promote efficient use of antibiotics, an Antibiotic Therapy Commission is to be set up at the Robert Koch Institute (RKI). Among other things, it will be responsible for reviewing recommendations relating to antibiotic therapy and initiating their elaboration. Moreover, measures are to be introduced for improving diagnostics, as well as the basic training, specialist training and continuing education of physicians and pharmacists, nursing staff and scientists in this field.

III. Promoting cooperation

If prevention and control measures for reducing antimicrobial-resistant pathogens are also to be successful in the long term, the regional and national players in this sector need to cooperate. Based on previously established prevention and control strategies, regional networks for preventing and controlling antimicrobial resistance are to be set up as pilot projects, and collaboration between regional players in this field is to be intensified. At the federal level, an Interministerial Working Group has been set up in the field of antimicrobial resistance to coordinate the actions on an interdepartmental basis and ensure a dialogue between affected players. In addition, a Centre for the Prevention and Control of Antimicrobial Resistance is to be established at the RKI at the federal level. At the specialist level, the Centre is to assume a coordinating role in the field of human medicine and safeguard Germany's cooperation with international specialist agencies.

IV. Research and evaluation

Inappropriate use of antibiotics can be the result of numerous factors. Consequently, studies are to be conducted with the aim of examining in detail the decisive factors in Germany and the tools or supporting measures that physicians would like to see in order to promote efficient antibiotic therapy.

To support research, the current situation is additionally to be analysed, and the possibilities for further strengthening research are to be examined.

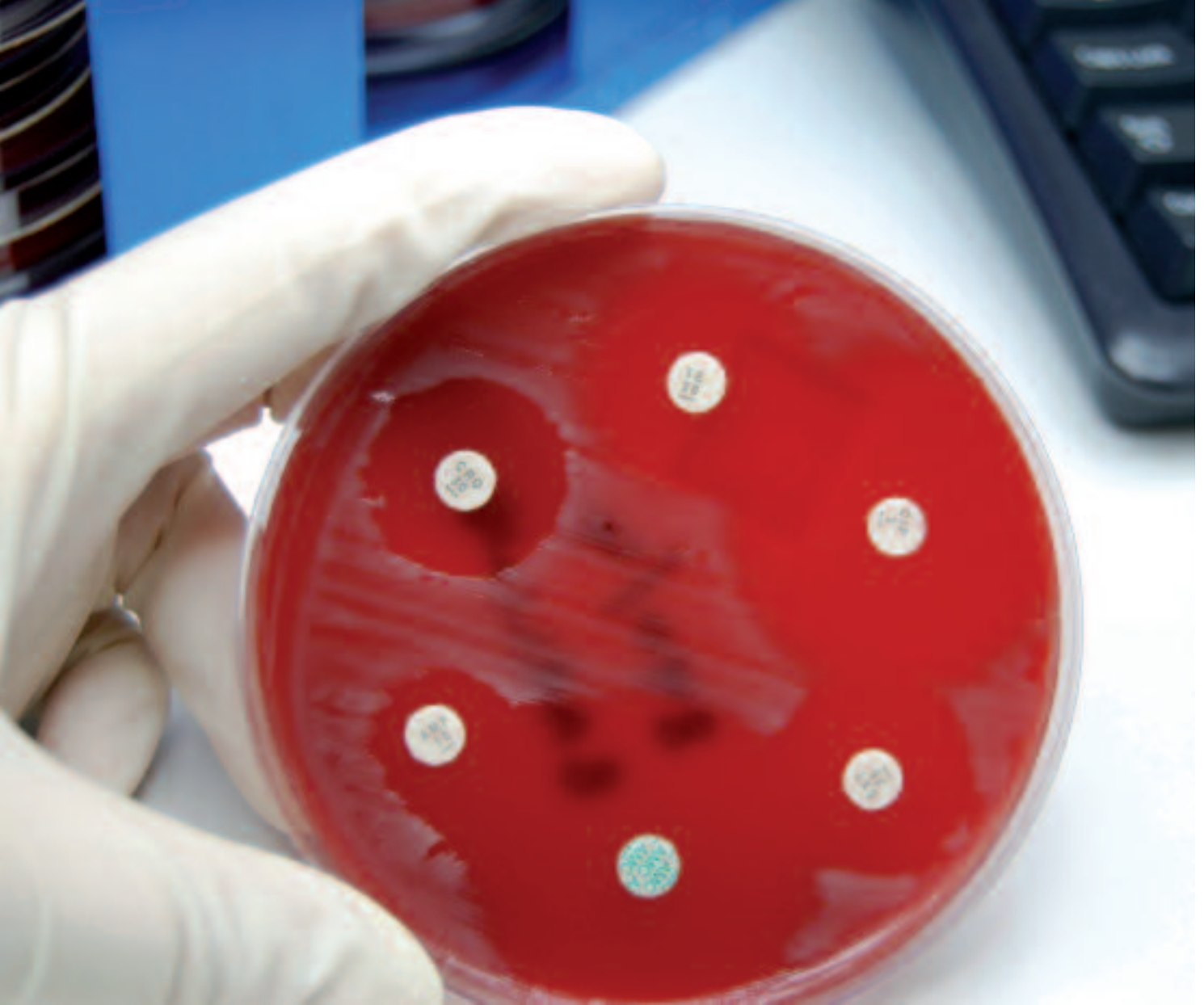
1.2 Veterinary medicine

Infectious diseases are of similar importance in animal health as in the field of human medicine. In addition, infectious diseases in agricultural livestock cause serious economic losses. In the field of veterinary medicine, the occurrence and spread of resistances in bacteria pathogenic to humans and animals is to be reduced in the framework of the Antimicrobial Resistance Strategy. Responsible use of antibiotics is intended to ensure the protection of consumer health, but without impairing animal health.

In particular, the following are to be achieved by the strategy for the field of animal husbandry, the food chain and veterinary activity:

- Comprehensive recording of the antimicrobial resistance situation,
- Continuous monitoring of the development of the antimicrobial resistance situation,
- Scientifically sound derivation of management measures,
- Improved information of veterinary surgeons, farmers and consumers,
- Widespread acceptance and implementation of the management measures in veterinary medicine and animal husbandry,
- Minimisation of antibiotic use, together with improved prophylaxis and hygiene to prevent infectious diseases, and
- An antimicrobial resistance situation that makes it possible to preserve the efficacy of antibiotics in the future.

The present Antimicrobial Resistance Strategy supports targeted measures for monitoring, controlling and avoiding antimicrobial resistance in Germany. Implementation of the goals it contains, and of the associated actions, necessitates the cooperation and support of the responsible players in this sector. Only a joint strategy, supported and implemented by the affected groups, can efficiently contribute to containing the problem.



2 Principles of antimicrobial resistance

2.1 What is antimicrobial resistance?

Antibiotics are substances used to treat bacterial infections. Their action is characterised by selective toxicity, since they interact with bacterial target structures. Even small quantities are capable of inhibiting bacterial growth or killing the bacteria. If the antibiotic has no effect on the bacteria, this is referred to as antimicrobial resistance (or also antibiotic resistance), i.e. the antibiotic cannot be used for treatment.

A distinction is made between natural and acquired antimicrobial resistance. In the case of natural resistance,

there are no changes in the bacterial genotype. The antibiotic nevertheless has no effect because, for example, the size of the antibiotic molecule is such that it cannot pass through the bacterial cell wall and is thus unable to reach the site of action in the bacterium.

Acquired resistance is based on changes in the bacterial genotype, which can arise due to what are known as mutations or through the acquisition of resistance genes. Resistance genes contain the genetic information of the antimicrobial resistance and are, for example, responsible for the formation of additional enzymes and efflux pumps that inactivate the antibiotic or transport it out of the bacterial cell.

In contrast to natural resistance, acquired resistance is highly variable and can in principle be transferred by transmission of the resistance genes to other bacteria. The exchange of resistance genes between different species of bacteria can lead to the development of multiresistant pathogens. Hospitals are frequently critical locations, where these multiresistant pathogens occur in elevated numbers because different pathogens are present in high concentrations there and can undergo selection as a result of the high level of antibiotic use. In addition to methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococci (VRE), increasing attention has in recent years been demanded by multiresistant Enterobacteriaceae, *Pseudomonas* and *Acinetobacter*. Serious infections resulting from resistance development in these and other, previously seldom observed pathogens, such as *Clostridium difficile*, frequently make treatment difficult. This also applies to patients in long-term care facilities. In addition, inconsistent decolonisation of MRSA patients in these facilities can lead to the development of reservoirs for multiresistant pathogens. Furthermore, pathogens having multiple resistances and elevated virulence are increasingly being observed in the general public, especially in connection with organisms causing pneumonia (*Streptococcus pneumoniae*) and community-associated MRSA, and also *Escherichia coli* as a pathogen causing urinary tract infections.

2.2 Causes of resistance development

Resistances develop, for example, as a result of the interplay between resistance-mediating genetic events (mutation or absorption of “resistance genes”) and selection. Genetic events occur all the time, at a low rate. The selection pressure exerted by the use of antibiotics determines whether they have an effect in terms of resistance development.

One important cause of the increase in resistance development is the indiscriminate prescribing of antibiotics in human medicine. Antibiotics are often prescribed for viral infections (especially respiratory tract infections), although they are only effective against bacterial infections.^{58,66} In other words: antibiotics are frequently used without a confirmed indication and without prior diagnosis, partly because patients specifically ask for an antibiotic.¹⁰⁴

In addition, so-called broad-spectrum antibiotics are often used against bacterial infections for which narrow-spectrum antibiotics would be sufficiently effective. The widespread use of these antibiotics promotes selection, and thus also the spread of multiresistant pathogens. In the worst-case scenario, this can lead to broad-spectrum antibiotics no longer being effective because the bacteria have become resistant to the available antibiotics.

Another reason for the constant increase in antimicrobial resistances in Germany is probably the incomplete knowledge of physicians and nursing staff regarding the antimicrobial resistance problem. The subject is sometimes given only very brief treatment in basic medical training, specialist training and continuing education, which can result in antibiotics being used inappropriately and recommendations on hygiene and infection prevention not being sufficiently observed. This can lead to resistance development and the spread of resistant pathogens in medical facilities, meaning that resistance rates can then rise very rapidly.

Apart from incomplete knowledge of the antimicrobial resistance problem, there are numerous other influencing factors and causes, such as fears of possible liability and compensation claims if antibiotic treatment is not given, or the patient's request for an antibiotic. As a result, antibiotics may be used inappropriately or excessively.¹⁰⁴ Moreover, knowledge of the antimicrobial resistance problem alone is not enough to change behavioural patterns and bring about the application of recommendations and guidelines in this field.

The unreliable intake of antibiotics by patients can likewise encourage the development of antimicrobial resistances.

Furthermore, antibiotic metabolites (breakdown products) and resistant pathogens get into sewage via faeces. Some antibiotic metabolites can lead to the development of resistances in bacteria in sewers and sewage treatment plants, owing to the permanent selection pressure existing there. In addition, antibiotics are discharged directly into the environment, where new resistances can then develop in open waters and in the soil.

Consequently, there is a need to develop a joint strategy incorporating all the affected fields.

2.3 What is the problem with antimicrobial resistance?

Immediately after the first antimicrobial substances were introduced in the 1930s and 1940s, the first pathogens began to display resistance to them. As soon as the 1950s and 1960s, there was an increase in resistance to antibiotics that had been in use since the late 1940s. As a result, broad-spectrum antibiotics are used, often unnecessarily, which again lead to selection of resistant pathogens and induce a further increase in the rate of resistant pathogens. Attention must be paid to the problem of cross-resistance and parallel resistance in this context. Due to the fact that gene segments responsible for several resistances are located on certain genetic units, such as resistance plasmids, selection for one resistance simultaneously encourages resistance to other antibiotics.

At the same time, the ageing population and the growing use of invasive measures in modern medicine, e.g. surgery, will probably lead to a further rise in the demand for antibiotics. The resultant consequences for patients are possibly ineffective therapy, a longer duration of treatment, and curing of the infection that is delayed or possibly fails to materialise at all, sometimes with a fatal outcome. Moreover, substantial additional costs are incurred by the health system. The cost per infection caused by resistant pathogens can be more than twice as high as for infections caused by sensitive pathogens. These costs result from increasing medication costs, additional nursing effort and a longer stay in hospital for the affected patients.^{71,124}



3 International situation in the field of antimicrobial resistance

The rise in antimicrobial resistance in recent years is viewed with concern worldwide. Increasing resistance to antibiotics, particularly of pathogens responsible for respiratory infections, has in the past few years led to growing uncertainty among the public and also among physicians and the responsible players in the health system. As a reaction to this development, various organisations have launched initiatives and strategies for containing antimicrobial resistance.

In 2001, both the WHO and the European Commission published strategies for avoiding bacterial resistance to antibiotics.^{12,128} Both strategies emphasise the importance of regional, national and international microbial surveil-

lance strategies for control. Both the WHO and the EU initiated the establishment of international resistance monitoring systems.

Since 2001, the EU Member States have been sending resistance data to the EARSS (European Antimicrobial Resistance Surveillance System, see also Appendix 1.3.1). The EARSS resistance data show very low resistance rates in the Scandinavian countries and the Netherlands in relation to such pathogens as methicillin-resistant *Staphylococcus aureus* (MRSA) or vancomycin-resistant *Enterococci*. Southern European countries, such as Portugal and Greece, have the highest resistance rates for these pathogens and lead the field by far in a European com-

parison. The data from France reveal that MRSA rates there have been declining since introduction of the French strategy for safeguarding the effect of antibiotics.³⁴ Germany comes in the middle of the field in a European comparison. Some resistances, such as MRSA, rose steadily from 1999 to 2004, since when a constant resistance rate in the region of 20 % has been observed. In contrast, the resistance rate for fluoroquinolone-resistant *E. coli* has continued to rise, from 4 % in 1999 to 29 % in 2006.³⁸

The EU additionally initiated establishment of the European ESAC network (European Surveillance of Antimicrobial Consumption) to monitor the consumption of antibiotics in the outpatient sector.

These data show that Portugal and Greece have a high level of antibiotic consumption, while the Netherlands have the lowest level of antibiotic use.⁵⁶ Germany has moderate to low antibiotic consumption in the outpatient sector in a European comparison. Compared to other European countries, however, reserve antibiotics (antibiotics with a very limited indication) and broad-spectrum antibiotics are prescribed more frequently in Germany.¹²

These data reveal a correlation between the national use of antibiotics in the outpatient sector and the different national resistance rates in Europe. The differences in selection pressure, i.e. the different levels of antibiotic consumption, lead to different resistance rates in the individual countries.⁵⁷

The growing spread of antimicrobial-resistant pathogens makes it increasingly difficult to treat infections caused by (multi)resistant pathogens.⁵⁷ The lack of new antibiotics and diagnostic (rapid-test) methods for identifying (multi)resistant pathogens is likewise leading to an increase in resistance rates. Rapid identification of resistant pathogens permits early, targeted action, and the indicated use of new antibiotics could contain resistant pathogens.

The problem is that the pharmaceutical industry is increasingly withdrawing from research in this field, both internationally and in Germany.³⁶ The underlying reasons for this are the high development costs, which frequently take too long to recover since – compared to cardiovascular drugs, for example – antibiotics have limited indications and are only prescribed for a short period. Moreover, the development of antibiotics tends to be impeded by restriction of the indications for new antibiotics.

This problem could be solved by strategic partnerships between scientific institutes and the pharmaceutical industry,⁵⁷ although greater commitment on the part of the pharmaceutical industry would be a fundamental prerequisite in this context.

Although many countries have higher antimicrobial resistance rates and higher antibiotic consumption than Germany, there are also countries, such as Denmark and the Netherlands, that are in a better position in a European comparison. The success of the antimicrobial resistance policy of these countries shows that the situation in Germany can also be improved. The measures required for this purpose will be presented after a description of the German situation.



4 German situation in the field of anti-microbial resistance

When considering all the existing measures and activities for recording and analysing data on antimicrobial resistance and on antibiotic consumption, as well as on the prevention and control of antimicrobial resistance in human medicine (presented in detail in 1.3), it can be seen that there are duplications and gaps in different sectors. Collected data are not pooled, or not fed back to prescribing physicians, and there is no top-level coordination of activities. There now follows a more detailed description of the situation in the individual sectors.

4.1 Human medicine

4.1.1 Antimicrobial resistance data

Data on antimicrobial resistance are available in various surveillance projects (see also Appendix 1.3.1). However, these data are hard to compare, and the majority of them are only available locally. The institutions leading the surveillance projects differ greatly as regards their levels of responsibility and action. In addition, the projects use different diagnostic methods and assessment criteria, or they are not documented. Furthermore, some projects

provide no information regarding quality control, and thus on the quality of the data. Germany has no nationally uniform specifications regarding how data on antimicrobial resistance should be recorded and analysed. The surveillance data available in Germany to date relate to individual species of pathogen, individual antibiotics and heterogeneous patient populations. Urgently necessary for an early-warning system are data on the occurrence and spread of infections involving multi-resistant pathogens for which there are only limited therapy options, or none at all.

The greater part of the data available in Germany describe the antimicrobial resistance situation in maximum-care hospitals. Only very limited data are available from the field of private practice and from hospitals providing basic and standard care. Consequently, no statements can be made as regards the antimicrobial resistance problem in these healthcare sectors. However, even the currently available data from maximum-care hospitals do not permit a representative, nationwide assessment of this sector. The German Network for Antimicrobial Resistance Surveillance (GENARS) provides good data on antimicrobial resistance, compiled on the basis of excellent diagnostics. However, only six university hospitals are currently involved in GENARS. Combined with the data collected for the EARSS network, these data cover a total of just 2 % of Germany's population. As a result, Germany, the country with the highest population, takes last place among the total of 30 EARSS participants in terms of representativeness.⁶⁹

A representative surveillance system for the outpatient and inpatient sectors is needed as a basis for localising problem areas in Germany, and also for comparing resistance rates at the national and international level.

The situation in the outpatient and inpatient sectors differs greatly. High antibiotic consumption in the inpatient sector leads to high selection pressure and can lead to high resistance rates in hospitals. The situation in the field of private practice is probably less serious. However, there has also been an increase in the number of resistant pathogens in the outpatient sector in recent years. An appropriate early-warning and response system for the outpatient and inpatient sectors is necessary in order to be able to monitor this trend and future developments.

Knowledge of the changes occurring in resistance development in the outpatient and inpatient sectors is important, so that these changes can be taken into considera-

tion in antibiotic therapy. Consequently, there is a need for a systematic procedure for feeding back antimicrobial resistance rates to the prescribing physicians. So far, this only exists to a very limited degree in Germany.

4.1.2 Antibiotic consumption data

Analysed data on antibiotic consumption in hospitals are so far available only in isolated cases (see also Appendix 1.3.2), although most hospital dispensaries record data on antibiotic consumption. However, these data are recorded with an eye to economic aspects, i.e. the costs of the prescribed antibiotics are compiled, not the quantities prescribed.

It is estimated that antibiotics prescribed to inpatients account for a share of between 5 % and 20 % of all prescribed antibiotics.³⁶ Thus, the greater part (80% to 95%) is prescribed in the out-patient sector. Available data show that antibiotic consumption in the inpatient sector primarily depends on the clinical discipline and less on the size of the hospital. The highest antibiotic consumption is seen on intensive-care and haematological-oncological wards.^{35,36} The SARI project (Surveillance of Antimicrobial Use and Antimicrobial Resistance in Intensive Care Units) was able to show that feeding back the consumption data to the prescribing physicians is capable of achieving a reduction of up to 30 % in antibiotic consumption in some cases.⁸⁷ The total antibiotic consumption of the participating intensive-care wards showed no significant rise in the period 2001 to 2004, although there was an increase in the percentage of broad-spectrum antibiotics prescribed and in resistant pathogens.⁹¹ The consumption data available for the inpatient sector are, however, not representative for Germany.³⁶

According to extrapolations by the Scientific Institute of the Local Health Care Funds (WIdO), roughly 250–300 tonnes of antibiotics were used in the outpatient sector of human medicine in 2004.²² Outpatient antibiotic consumption in Germany has been stable since 1991, and declining slightly since 2001, although broad-spectrum antibiotics are accounting for an increasing share of total consumption. Regional antibiotic consumption differs within Germany. Almost twice as many antibiotics are prescribed in Western Germany (Rhineland-Palatinate) as in Eastern Germany (Brandenburg).^{112,113} The reason for this is unknown. However, consumption could be reduced further for certain indications in the outpatient sector. Studies reveal that antibiotics are prescribed to up to 80 % of patients with common colds, which are usually caused by

viruses.^{58,66,95} However, it is also not always necessary to use antibiotics to treat bacterial infections, e.g. some diarrhoeic illnesses.⁹⁵

The antibiotic consumption data compiled and analysed by the WIdO provide a very good description of consumption in the outpatient sector. They are representative for Germany and are prepared on the basis of the prescription accounts at the expense of all statutory health insurance funds.

These data are available generally and compiled regularly.⁹⁴ Moreover, the data are also fed back to prescribing physicians in monthly prescription reports.¹¹⁴ In addition, individual medical consulting can help physicians get an assessment of their own prescribing practices.⁸⁴ In this context, their own prescription data can be critically compared with the prescription data of other physicians in a reference region, or of a reference specialist group, thus leading to a reduction in the number of antibiotic prescriptions.

The consumption data provide no information regarding the indication-oriented use of the antibiotics. Critical diagnosis and indication-oriented use would lead to a further reduction in antibiotic consumption.¹¹³

4.1.3 Recommendations and guidelines for preventing and controlling antimicrobial resistance

Numerous recommendations and guidelines exist in Germany regarding the control and avoidance of antimicrobial resistance (see also Appendix 1.3.3), but certain resistance rates are nevertheless continuing to rise in Germany. Inconsistent application of the aforementioned recommendations and guidelines is part of the reason for this. For instance, actual compliance with guidelines for optimising antibiotic therapy on intensive-care wards reaches only 20 %–30 %.¹¹⁷ Consequently, there is a need not only to introduce recommendations and guidelines, but also to comply with them and evaluate their application. To make compliance easier for users, it is important to provide user-friendly standards that are readily accessible to everyone. Moreover, standards must be reviewed at regular intervals, and also modified in keeping with the local resistance situation.

To prevent unnecessary use of antibiotics, a diagnosis must be made critically and the necessity of antibiotic therapy determined. Recommendations and guidelines on diagnosing infectious diseases and on antibiotic therapy can help promote the appropriate use of antibiotics in

this context. However, recommendations and guidelines are developed and propagated by different interest groups. There is additionally the risk of economic interests influencing professional recommendations.

Antibiotics are prescribed in almost all medical disciplines. In the expert sector, there are many different groups that are in turn united in different scientific societies. These scientific societies focus on a disease, a medical discipline, or also several medical disciplines. This makes it more difficult to jointly elaborate coordinated recommendations on the diagnosis and antibiotic therapy of diseases.

In Germany, uniform, independent and professionally sound recommendations and guidelines on the diagnosis of infectious diseases and on antibiotic therapy exist only for selected diseases, such as community-acquired pneumonia (see Appendix 1.3.3.1 for an overview).⁷³ It is often known only in isolated cases whether such recommendations are consulted as the basis for local recommendations and (correctly) applied. Their application demonstrably has a positive effect on the course of therapy, its outcome and the curing or prevention of infections.^{37,117}

The antibiotic therapy recommended in local guidelines cannot always be applied owing to specific characteristics of the individual patient. Deviations may be necessary, particularly in the case of high-risk patients. In instances of this kind, advice from the local clinical microbiologist can make a helpful and supportive contribution to antibiotic therapy.

In addition, the hygiene and infection prevention recommendations of the Commission on Hospital Hygiene and Infectious Disease Prevention (KRINKO) are a significant help in controlling, avoiding and preventing the further spread of antimicrobial resistances;¹⁰⁸ the KRINKO infection prevention recommendations include infections due to (multi)resistant pathogens. However, there is frequently criticism that the recommendations are inadequately applied in practice.^{126,127} The introduction of suitable measures for increasing application of the recommendations is thus also important for reducing antimicrobial-resistant infective agents.

A number of recommendations and guidelines also exist in connection with quality assurance in laboratory medical studies.^{13–15} Among other things, these guidelines are intended to ensure that the results of resistance tests or identifications of infective agents are comparable. The “Chemotherapeutic Test Methods” Working Committee

of the Medical Standards Committee of the German Institute for Standardization (DIN) addresses the standardisation of methods for determining the susceptibility of infective agents. On the initiative of the DIN, a standard of the International Organization for Standardization (ISO 20776-1, 20776-2) has been elaborated and adopted that is now valid worldwide.¹¹⁰ Nonetheless, different methods and assessments are still used for resistance testing, also in Germany, making it difficult to compare the data.^{4,5,116,118} To counteract the unacceptable situation of there being different limits in Europe for interpreting resistance data, a Working Group of the European Society for Clinical Microbiology and Infectious Diseases (ESCMID) elaborated European limits (EUCAST),⁵⁰ which are in future to be incorporated into the marketing authorisation process and into the expert information on antibiotics.¹¹⁰

Uniform recommendations for resistance testing, and for the recording and assessment of data on antimicrobial resistance, are so far only available at the European level.³⁰

4.1.4 Basic training, specialist training and continuing education of medical occupational groups, pharmacists and natural scientists

Knowledge deficits among physicians prescribing antibiotics, and among nursing staff, as regards the antimicrobial resistance problem can be one reason for the inappropriate use of antibiotics and the spread of antimicrobial resistance.^{2,32} A sound knowledge of the antimicrobial resistance problem is particularly important for physicians, pharmacists, nursing staff and natural scientists working in this field. Corresponding anchoring of the problem in basic training, specialist training and continuing education (see also Appendix 1.3.3.2) lays the foundations for appropriate use of antibiotics and for controlling and preventing the spread of (multi)resistant infective agents. Placing greater emphasis on this subject in the basic training, specialist training and continuing education of the aforementioned occupational groups is an important supportive measure for reducing antimicrobial resistance in Germany.

4.1.5 Further supportive measures for preventing and controlling antimicrobial resistance

At the European level, the Netherlands are a model example in the human medicine sector as regards their low antimicrobial resistance rates and antibiotic consumption. Dutch antimicrobial resistance policy is characterised by a consistent, coordinated approach based on the “search and destroy” principle. This approach is being

analysed in the context of the Euregio project MRSA-net (see also Appendix 1.3.3.3). The MRSA-net is a regional network for protecting the population against MRSA infections in the Twente/Münsterland region. Initial results show that introduction of the measures in the framework of the MRSA-net was able to reduce the MRSA rate.

In particular, the network structure promotes an exchange of knowledge and technology between participating healthcare players, i.e. between physicians, nursing staff, patients, their relatives and other involved parties. Knowledge deficits are eliminated, recommendations and guidelines are revised on an application and target group-oriented basis, and their application within the MRSA-net is promoted. The resolution of the 79th Conference of Ministers Responsible for Health is also certainly to be welcomed in this spirit. It recommends the establishment of regional networks involving all the players in the health sector for reducing MRSA infections and the spread of MRSA (see Appendix 1.3.3.3). However, the restriction of the networks to the MRSA problem should be regarded as a first step, and expansion to include further (multi)resistant pathogens targeted.^{31,60}

EU Member States are increasingly initiating public campaigns addressing the problem of anti-microbial resistance. Successful examples from France and Belgium show that they can make an important contribution to educating the population. Patients' requests regarding the prescribing of antibiotics, and their correct intake, have an influence on antibiotic consumption.¹⁰⁴ Education campaigns could improve patients' knowledge in these areas and contribute to reducing antibiotic consumption.

Hardly any public campaigns on this subject have been implemented for the general population in Germany (see also Appendix 1.3.3.4). There is so far also no knowledge regarding the degree of influence exerted on physicians by patients when antibiotics are prescribed, or of the extent to which antibiotics are taken inappropriately by patients in Germany.

4.1.6 Research

4.1.6.1 Research activities on antimicrobial resistance in the portfolio of the BMG

The RKI conducts research in the field of antimicrobial resistance in various disciplines; studies and projects are implemented both by individual disciplines and jointly on an interdisciplinary basis, as well as with external partners in some cases. Six research areas of the RKI in the field of antimicrobial resistance are presented below.

I. Antimicrobial resistance and antibiotic consumption surveillance

Surveillance is being reorganised under the designation ARS (Antimicrobial Resistance Surveillance in Germany) as the basis for research into the development of antimicrobial resistance and the emergence of new resistances. Clinically relevant bacterial pathogens are continuously documented in inpatient and outpatient healthcare according to a standard survey plan. It is in future also to be possible to make statements regarding structural features of patient care, the epidemiological situation and the development of antimicrobial resistance over time. The investigation of specific questions in studies permits detailed analysis and the targeted introduction of preventive measures.

II. Studies of antibiotic prescribing and patients' attitudes towards antibiotics

A further area of research involves studies on the prescribing of antibiotics and patients' attitudes towards antibiotics.

Promoting the appropriate use of antibiotics calls for knowledge of the factors influencing, and the reasons for, the prescribing of antibiotics by physicians in hospitals and in private practice. These factors influencing the prescribing of antibiotics by physicians in Germany are to be examined in the framework of a study.

Knowledge, attitudes and expectations of the public in relation to antibiotics and the prescribing of antibiotics are being examined in a further study.

III. Pathogens with special resistances

Research in this area focuses on the molecular characterisation of pathogen strains, their resistance genes and their mobile genetic elements. In addition, studies are carried out regarding the emergence and spread of strains displaying multiple resistance and new resistance characteristics.

IV. Molecular biology, hygiene and epidemiological research into *Clostridium difficile*

Both the distribution of *Clostridium difficile* in the hospital population and transmission routes in hospital are being investigated in the framework of a multi-centre study of *C. difficile* in hospitals in the Berlin/ Brandenburg region.

Owing to high regional concentrations in Southwest Germany, epidemiological studies are being conducted to examine temporal trends and risk factors in

connection with severe courses of *C. difficile* infections, as are molecular biology investigations regarding the occurrence and spread of fluoroquinolone-resistant hospital strains.

V. Ecological studies on antimicrobial resistance

Interdisciplinary ecological studies are implemented in the following areas:

- Horizontal resistance gene transfer,
- Spread of antimicrobial resistance in *Salmonellae*,
- Determination of the colonisation of veterinary surgeons and veterinary staff with MRSA as a function of exposure.

VI. Prevention of nosocomial infections

The following scientific work is performed in this area:

- Survey of antibiotic use and elaboration of infection prevention concepts in homes for inactivating relevant pathogens causing nosocomial infections,
- Establishment of regional networks for intensifying prevention measures for avoiding the further spread of (multi)resistant pathogens,
- Together with the KRINKO, establishment of evidence-based prevention strategies for nosocomial infections.

4.1.6.2 Need for research and development

The Joint Scientific Advisory Board (GWB) of the BMG addressed the need for research into antimicrobial resistance in the framework of a workshop at the RKI. This workshop was attended by some 40 experts. Six working groups analysed deficits and fields of action in the sphere of antimicrobial resistance research. A joint final discussion defined the following deficits to be eliminated with priority in the individual areas:

1. Social science and public health studies

- Survey of the population regarding antibiotic use, interaction with physicians, intake patterns, attitudes towards antibiotics
- Analysis of existing data (e.g. KIGGS, routine pharmacoepidemiological data, individual patient data) on antibiotic use in different social strata, assessment of the quality of antibiotic prescribing
- Behavioural psychology research for improving hygiene-related behaviour in hospitals/ prevention of the transmission of antimicrobial resistances
- Evaluation of continuing education methods for physicians regarding the prescribing of antibiotics

2. Healthcare-oriented research

- Optimisation of surveillance, particularly in the out-patient sector
- Outcome-oriented intervention studies (antibiotic use, hygiene measures)
- Clostridium difficile-associated diarrhoea (CDAD network)
- Transmission studies, persistence studies

3. Molecular epidemiology

- Implementation of the results of genomics for pathogen typing and characterisation
- Development and establishment of methodological platforms and central databases, including bioinformatics
- Clarification of population structures (composition and dynamics of infective agents in relation to the development of antimicrobial resistance)
- Studies on the importance of antibiotic use for the microecology of bacterial populations in colonisation habitats (intestinal flora, cutaneous flora)
- Studies on the macroecology of antimicrobial resistance (timely detection of the emergence of "new resistances")

4. Clinical microbiology

- Determination of risk factors (morbidity, physician-related factors) for regionally high out-patient antibiotic consumption
- Determination of protective factors (structural, process-related factors in the field of hygiene and in the field of antibiotic management, case mix) for low rates of nosocomial infection by resistant pathogens and of defined complications of infections
- Development and validation of controllable indicators (including microbiological diagnostics) for appropriate antibiotic use
- Development and clinical validation of rapid tests (confirmation of pathogen and/or resistance, biomarkers)

5. Molecular foundations of antimicrobial resistance

- Adaptation mechanisms of bacteria (resistogenomics and pathogenomics), evolutionary aspects of resistance and transfer, rapid diagnosis of resistances
- Development of antibiotics that impede resistance development

- In vivo studies of virulence and growth mechanisms, and of interaction with the human immune system
- Systemic biology analysis of resistance

6. Development of vaccines against multiresistant pathogens

- Development of passive and active vaccines against *S. aureus* and other multiresistant nosocomial pathogens
- Development of effective vaccines for immunocompromised and elderly patients
- Development of new vaccination strategies to improve mucosal protection
- Development of informative animal models and surrogate markers

4.1.7 Necessity of a national, interdisciplinary strategy

The development of antimicrobial resistance is a complex process and influenced by numerous factors. Given rising resistance rates in Germany, there is an urgent need for action. Monitoring, controlling and minimising antimicrobial resistances requires a coordinated strategy that initially focuses on interventions in certain areas. The example of France clearly shows that the introduction of a coordinated national strategy is capable of successfully reducing antibiotic consumption and antimicrobial resistance rates.⁶⁸ Particularly the extensive education and information of the public, and of physicians in private practice, in France has so far led to a 13.3 % decline in the prescribing of antibiotics since the French strategy was introduced.³⁶

The European Commission also demands the development of a national strategy. In its Recommendation on the prudent use of antimicrobial agents in human medicine, the EU calls upon the Member States to introduce specific strategies for the prudent use of antimicrobial agents in order to contain antimicrobial resistance.²⁷

Therefore, a national strategy has been developed for detecting, preventing and controlling antimicrobial resistances. It is designed to permit top-level coordination, evaluation and expansion of activities, and to guarantee a coordinated approach when tackling existing and/or new problems in the field of antimicrobial resistance. To ensure that the strategy covers every essential aspect, relevant players were called upon to take active part in devising the strategy.

4.2 Veterinary medicine

4.2.1 Importance of antimicrobial resistance for the field of animal husbandry, the food chain and veterinary activity

Antimicrobial resistance is a significant problem for public health and thus also has an impact on the field of animal husbandry, the food chain and veterinary activity. Antibiotics are, however, indispensable for treating sick animals and animal stocks. Occupation with the subject of antimicrobial resistance consequently has an impact on consumer protection, animal protection and animal health as aims of the BMELV. Every use of antibiotics in human medicine, veterinary medicine or plant protection can lead to the development of resistances. Moreover, substances that have antibiotic action, but are used with a different objective in mind (e.g. certain mycotics or coccidiostats and histomonostats), can likewise lead to the development of resistances due to their influence on the omnipresent bacterial flora.

On the one hand, the resistances occurring in veterinary medicine have direct effects on animal health in that they can negatively impact the efficacy of veterinary medicinal products (antibiotics). This gives rise to direct consequences for the treatment both of agricultural livestock and of “hobby” animals (e.g. pets and small animals) that need to be considered in veterinary medicine and can lead to problems when treating infectious diseases. The consequence can be restricted availability of effective antibiotics for veterinary medicine, and thus deficits in animal protection.

On the other hand, the emergence of antimicrobial-resistant pathogens in animals is also of direct significance for man and human health. The possibility of transmission of bacteria (pathogens and commensal organisms) displaying antimicrobial resistances to persons working in animal husbandry (e.g. farming) or to animal owners (e.g. “hobby” animals, animals as members of the family, pets and small animals) cannot be ruled out. Moreover, transmission to humans through foods of animal origin is also possible, if they are contaminated with bacteria that are resistant to antibiotics or bear antimicrobial resistance determinants.

Similarly, the pathogens excreted by animals are released into the environment. There are signs that the existing pool of resistance genes grows in the environment, and that the passing-on of resistance genes is promoted in this way.

4.2.2 Aims of the Antimicrobial Resistance Strategy for the field of animal husbandry, the food chain and veterinary activity

The Antimicrobial Resistance Strategy for the field of animal husbandry, the food chain and veterinary activity is intended, in a cooperative effort of human medicine and veterinary medicine, to influence the use of antibiotics in animals and reduce the emergence and spread of resistances in bacteria that colonise humans or animals. The aim is that the strategy be acknowledged and put into practice by veterinary surgeons, farmers, animal owners, industrial associations and competent authorities. This strategy, and the handling of antibiotics in animal husbandry, reflect pan-European and international/supranational targets. In conjunction with existing antibiotics guidelines – which are currently being revised – responsible use of antibiotics in the field of animal husbandry, the food chain and veterinary activity is intended to ensure the protection of consumer health without impairing animal health. To this end, there is also a need for research and development work as regards improved animal husbandry, diagnosis and alternatives to the use of antibiotics.

The strategy is designed to achieve the following targets:

- Comprehensive documentation of the antimicrobial resistance situation,
- Constant monitoring of the development of the antimicrobial resistance situation,
- Scientifically sound derivation of management measures,
- Improved information of veterinary surgeons, farmers and consumers,
- Widespread acceptance and implementation of the management measures in veterinary medicine and animal husbandry,
- A reduction in antibiotic use, together with improved prophylaxis and hygiene to prevent infectious diseases, and
- An antimicrobial resistance situation that also makes it possible to preserve the efficacy of antibiotics in the future.

To achieve these targets, the measures already in existence are analysed and the need for action is described. In addition, research and development needs are derived. The strategy for achieving the targets listed must be seen as a dynamic process. To be able to verify the efficacy of the measures taken and to be taken, regular reports are to be submitted regarding the progress of the measures described. An open discussion with all affected groups is

to be held to this end. It may be necessary in future to specify new measures or amend the measures taken.

4.3 Environment

After use, antibiotics can get into the environment by a wide variety of routes, by far the greater part being discharged via sewage treatment plants. Also of significance in this respect is the discharge of resistant pathogens in the sewage from hospitals, for example. The possibility of this sewage having an undesirable effect on water and soil organisms cannot be ruled out. Antibiotics and resistant pathogens have already been detected in the discharge from sewage treatment plants and in surface waters.^{115,119}

However, antibiotics and resistant infective agents can also be released directly into the environment, e.g. from animal husbandry. Antibiotics are not readily biodegradable. This encourages resistance development resulting from increased discharge into the environment, and also the risk of resistant pathogens in the environment contributing to the problem of resistance development in infective agents.¹



5 DART in the field of human medicine

5.1 Principal goal of the strategy

The German Antimicrobial Resistance Strategy, **DART**, is intended to make a decisive contribution to reducing the number and spread of antimicrobial resistances in Germany. To achieve this goal, all the players involved are actively participating in the realisation of the national goals and cooperating closely with each other.

5.2 National goals

The national goals set forth the strategic orientation of the German Antimicrobial Resistance Strategy and define its key content. The goals are the basis for developing, maintaining or improving activities at the national, regional and local level, and for specifying fields of action, actions and milestones. All in all, the present strategy encompasses ten national goals, which are in turn grouped in four components:

- I. Surveillance systems for antimicrobial resistance and antibiotic consumption
- II. Prevention and control measures for reducing antimicrobial resistances
- III. Cooperation and coordination
- IV. Research and evaluation

In structural terms, this strategy design and the order of the national goals are geared to the recommendations of the European Council. Therefore, the design and the order of the goals do not permit any statement to be made regarding the importance of the individual goals. Actions and players are assigned to each goal, and a milestone is assigned to each action (an overview of the actions and milestones can be found in the Appendix). The actions are to begin or be completed by the respective milestones in order to achieve the goals.

COMPONENT I:

Surveillance systems for antimicrobial resistance and antibiotic consumption

GOAL 1

Strengthening of the surveillance systems for antimicrobial resistance and antibiotic consumption

Sub-goal 1.1: Strengthening of the surveillance systems for recording and assessing antimicrobial resistance

Requirement:

Representative surveillance system for the outpatient and inpatient sectors for assessing local, regional and national antimicrobial resistance in Germany, with central recording and analysis of the data.

Background:

At the local level, the surveillance of data on antimicrobial resistance from daily routine diagnosis permits assessment of the problem in local medical facilities, particularly by means of comparison with regional or national data. Surveillance reveals problems, making it easier to tackle and remedy or improve them in a (more) targeted manner. In addition, data on antimicrobial resistance provide information of importance for assessing the effectiveness of intervention measures introduced. The effect of an intervention measure can be examined by comparing the resistance rates before and after the intervention.

Moreover, knowledge of the local resistance situation reduces the risk of therapy failures, and the quality of patient treatment improves.

The national collection and presentation of local data on antimicrobial resistance permits central analysis of the data. These data are also to be accessible and usable for the scientific community. National data are important for producing national trend analyses and for international comparison. Pooling local data from routine diagnosis indicates whether resistance problems are locally defined or have supraregional dimensions. This makes it possible to react promptly to new and existing resistance problems.

Actions:

- Compilation of acknowledged recommendations for the recording and analysis of data on antimicrobial resistance
Milestone: By the end of 2009, under the management of the RKI
- Integration of existing surveillance projects with a general survey approach and based on existing structures, as well as establishment of a central database; recruitment of new participants, long-term support and maintenance of the database on surveillance of antimicrobial resistances
Milestone: Starting in 2008, at the RKI
- Review of data on antimicrobial resistance from existing surveillance projects with a specific survey approach as regards quality and comparability, and pooling of the data from these projects in annual reports
Milestone: By the end of 2009, under the management of the RKI
- Joint use of the antimicrobial resistance database by RKI/BfArM, and availability of the data to the scientific community
Milestone: Starting in 2010, RKI and BfArM
- Expansion of compulsory notification according to Section 7 Para. 1, first sentence, IfSG to include the detection of MRSA in blood or liquor and the detection of toxin A or B of *Clostridium difficile* in faeces
Milestone: By mid-2009

Participants:

BMG, RKI, NRZ, BfArM, Länder authorities, ÖGD, hospitals, (private) microbiological centres/ laboratories, outpatient practices, relevant research facilities, e.g. CAP-Netz coordinators

Sub-goal 1.2: Strengthening of the monitoring systems for recording and assessing antibiotic consumption

Requirement:

Representative monitoring system for the outpatient and inpatient sectors for assessing local and national antibiotic consumption for Germany, with central recording and analysis of the data

Background:

The monitoring of antibiotic consumption data permits comparison of the antibiotics prescribed in a region, on the national average, or in certain disciplines or on certain wards. This permits correlation of consumption and resistance data, and signs of possibly excessive or incorrectly indicated antibiotic use can be discovered, checked and, if appropriate, remedied.

Local antibiotic consumption data provide information on the quantitative prescribing practices of medical specialists or physicians in a region. In addition, correlation of local antibiotic consumption data with the local resistance situation permits qualitative statements regarding the prescribing practices of these groups. A rough assessment of the antimicrobial resistance problem can also often be made on the basis of antibiotic consumption.

Local antibiotic consumption data are also necessary for assessing the effectiveness of an intervention measure (e.g. training/continuing education or participation in a quality circle). They additionally offer sound arguments for decisions and recommendations.

The pooling of local antibiotic consumption data to obtain national data permits comparison within the various regions, specialist groups and different institutions in Germany, and also at the international level.

Actions:

- Compilation of acknowledged recommendations for the recording and analysis of data on antibiotic consumption

Milestone: By the end of 2009, under the management of the RKI in cooperation with the Freiburg Centre for Infectious Diseases and the National Reference Centre for Surveillance of Nosocomial Infections

- Review of data on antibiotic consumption from other monitoring projects (e.g. SARI and MABUSE) as regards quality and comparability, and pooling of the data from these projects in annual reports

Milestone: By the end of 2010, under the management of the RKI in cooperation with the Freiburg Centre for

Infectious Diseases and the National Reference Centre for Surveillance of Nosocomial Infections

- Recruitment of new participants, and long-term support and maintenance of the database on monitoring of antibiotic consumption

Milestone: Starting in 2009, at the RKI

- Introduction of voluntary antibiotic consumption monitoring in hospitals

Milestone: By the end of 2009, under the management of the BMG

Participants:

RKI, BfArM, G-BA, BQS, SHI, PKV, KBV, WIdO, IF, DKG, hospitals/hospital dispensaries, ADKA, Freiburg Centre for Infectious Diseases and the National Reference Centre for Surveillance of Nosocomial Infections

GOAL 2

Systematic feedback of data on antimicrobial resistance and antibiotic consumption

Sub-goal 2.1: Establishment of a feedback system

Requirement:

Systematic feedback of data on antimicrobial resistance and antibiotic consumption to physicians prescribing antibiotics

Background:

Data collected in the surveillance systems for antimicrobial resistance (Sub-goal 1.1) and antibiotic consumption (Sub-goal 1.2) must be passed on to the prescribing physician. Only if physicians have an overview of their prescribing practices and the local resistance problem can they give appropriate consideration to them when prescribing in future.

Feeding back resistance and consumption data to physicians prescribing antibiotics is capable of reducing antimicrobial resistance and antibiotic consumption, thereby achieving savings.

Actions:

- Survey of the participants in the antimicrobial resistance surveillance system and establishment of a feedback system

Milestone: By the end of 2009, at the RKI

Participants:

BMG, RKI, BfArM, BZgA, Länder authorities, ÖGD, hospitals, (private) microbiological centres/laboratories, outpatient practices, rehabilitation facilities and nursing homes, DKG, SHI, PKV, G-BA, IQWiG, KBV, BÄK, State Chambers of Physicians, Regional Associations of SHI-Accredited Physicians

Sub-goal 2.2: Expansion of the system of National Reference Centres

Requirement:

Needs-based completion of the system of National Reference Centres

Background:

Timely detection of the emergence and spread of multiresistant pathogens, of new types of resistance (resistance genes and resistance mechanisms) and of outbreaks requires not only surveillance of antimicrobial resistance data from routine diagnosis, but often also further diagnostic and/or molecular epidemiological studies.

Studies of this kind are part of the sphere of responsibility of the National Reference Centres. Among other tasks, National Reference Centres are commissioned with promptly establishing sensitive and complex, new molecular biological systems for diagnosing new pathogen variants, and with assuring the quality of these diagnostic methods. In this way, new pathogen variants can be detected promptly, and prevention measures introduced. This requires feedback of the study results and, where appropriate, the test methods used to the microbiological laboratories.

In Germany, National Reference Centres exist only for selected pathogens, meaning that advanced studies are so far only ensured for these pathogens. Existing deficits, e.g. regarding infections with enterobacteria or *Clostridium difficile*, are currently dealt with on a project basis for a limited time and with limited capacities. Further gaps, and the material and personnel requirements to be derived from them, need to be identified. Working on this basis, an institution is to be identified for implementing advanced studies. This is to be followed by expansion of the work capacities for advanced studies, so that these studies can be performed in accordance with requirements and at an internationally competitive level.

Actions:

- Identification of the work capacity for advanced diagnostics/studies of (multi)resistant pathogens for which no National Reference Centre currently exists
Milestone: By the end of 2009, under the management of the BMG
- Identification and appointment of an institution catering to the requirements for advanced diagnostics/studies of (multi)resistant pathogens
Milestone: By the end of 2009, under the management of the BMG

Participants:

BMG, RKI, NRZ, consultant laboratories, Infection Epidemiology Commission, scientific societies

Sub-goal 2.3: Establishment of an early-warning system

Requirement:

Early-warning system for (new) resistance problems

Background:

Strengthening the existing surveillance system for recording antimicrobial resistances at the RKI (see also Sub-goal 1.1) will, together with the expansion of advanced diagnostics for multiresistant pathogens (Sub-goal 2.2), enable timely detection of new pathogens and resistances in the outpatient and inpatient sectors. The information gained is to be used for prompt elaboration of therapy and hygiene recommendations and for the development of prevention strategies. Adapted to the respective resistance problem, they are to be prepared by the RKI in the framework of its statutory tasks and made available to the competent authorities and agencies, as well as the affected specialist circles, so that the necessary measures can be taken there.

Actions:

- Establishment of an early-warning system
Milestone: By the end of 2010, under the management of the RKI

Participants:

BMG, RKI, Länder authorities, ÖGD, NRZ, consultant laboratories, Infection Epidemiology Commission, scientific societies

Sub-goal 2.4: Introduction of quality indicators in the field of antimicrobial resistance

Requirement:

Cross-sectoral introduction and application of quality indicators for antibiotic use and antimicrobial resistance

Background:

The introduction and application of quality indicators in the field of the antibiotics problem can contribute to quality assurance, and thus also to controlling antimicrobial resistances.

According to Section 91 of Book V of the German Social Security Code (SGB V), external quality assurance, measures for improving quality, and patient information is part of the sphere of responsibility of the Federal Joint Com-

mittee (G-BA). According to Section 137 Para. 1, first sentence, No. 1, the G-BA is authorised to define obligatory measures for quality assurance according to Section 135a and the fundamental requirements for institution-internal quality management. In cooperation with the institution according to Section 137a (BQS successor organisation), “cross-sectorally coordinated indicators and instruments” are to be developed that permit the “measurement and presentation” of the quality of services in all healthcare sectors. The G-BA furthermore defines the content of the Quality Report to be published at intervals of two years (Section 137 Para. 3, first sentence, No. 4). According to Para. 2, the guidelines according to Section 137 that the G-BA issues are to be of a cross-sectoral nature.

Actions:

- Development of indicators for antibiotic use and antimicrobial resistance
Milestone: Starting in 2009
- Examination of integration of the indicators in the external quality assurance of the institution according to Section 137a and in the Quality Report according to Section 137, Para. 3, first sentence, No. 4
Milestone: Starting in 2009
- Introduction and application of quality indicators, e.g. in the framework of the AQIUK project (Outpatient Quality Indicators and Indices) of the KBV
Milestone: Starting in 2009

Participants:

G-BA, KBV, institution according to Section 137a, KRINKO, BÄK, AkdÄ, LÄK, ÄZQ, German Coalition for Patient Safety, BMG, RKI, scientific societies

COMPONENT II:

Prevention and control measures for reducing antimicrobial resistances

GOAL 3

Promotion of the application of guidelines

Sub-goal 3.1: Development of guidelines

Requirement:

Generally acknowledged guidelines and recommendations for antibiotic therapy

Background:

International studies show that up to 50 % of all courses of antibiotic therapy given are inadequate, e.g. due to unsuitable doses or treatment periods.^{32,103} Recommendations and guidelines help medical staff when selecting and dosing an antibiotic and diagnosing infectious dis-

eases. The quality of healthcare services and treatment can be improved by recommendations and guidelines, thereby increasing patient safety.

Hardly any studies on the (correct) application of recommendations and guidelines for antibiotic therapy have been carried out in Germany to date.¹¹⁷ The application of recommendations and guidelines, and their value, are improved if the recommendations are evidence-based, coordinated with scientific societies/groups and adapted to local conditions.

Local recommendations are to be based on national, professionally sound recommendations and guidelines for antibiotic therapy. The review of existing recommendations and guidelines for antibiotic therapy, and initiation of the preparation of necessary new ones, is in future to be handled by an expert committee at the RKI. To this end, an Antibiotic Therapy Commission is to be set up, similar to the commissions already existing at the RKI. This Commission is also to be responsible for preparing general principles for antibiotic therapy, formulating a professional assessment of the antimicrobial resistance problem and advising the Interministerial Working Group on Antimicrobial Resistance.

The nationally uniform guidelines are to serve as a basis for preparing local recommendations. Local recommendations are necessary on the basis of the local resistance situation.

At the local level, the heads of medical institutions are to be responsible for the preparation of internal or local guidelines for antibiotic therapy. The relevant medical disciplines and players in the hospital are to be involved in preparing the guidelines, also giving consideration to the local antimicrobial resistance situation. This is intended to encourage application of the recommendations and guidelines. Taking the outpatient situation into account, comparable recommendations are also to be drawn up for the outpatient sector.

Easy access to the national and local recommendations and guidelines is of decisive importance for their application. Compliance with the recommendations and guidelines is to be supported by constant updating and adaptation. It is additionally to be examined whether and to what extent the introduction of quality indicators can support the preparation, introduction and application of local guidelines in hospitals.

Actions:

- Establishment of an Antibiotic Therapy Commission at the RKI

Milestone: By mid-2009, under the management of the BMG

- Preparation of general principles for antibiotic therapy, compilation of nationally acknowledged recommendations and guidelines, initiation of the preparation of necessary guidelines

Milestone: Starting in 2010, by the Antibiotic Therapy Commission at the RKI

- Evaluation of the application of recommendations for antibiotic therapy

Milestone: Starting in 2013, under the management of the RKI

Participants:

BMG, RKI, BfArM, Antibiotic Therapy Commission, scientific societies, German Medical Association, State Chambers of Physicians, SHI, PKV, G-BA, IQWiG, KBV, Regional Associations of SHI-Accredited Physicians, ÖGD, hospitals, outpatient practices, rehabilitation facilities and nursing homes, AKdÄ, KRINKO, ÄZQ

Sub-goal 3.2: Promotion of structures for applying guidelines and recommendations

Requirement:

Strengthening of structures for improving cooperation between responsible organisational units in hospitals

Background:

According to Section 135a in conjunction with Section 137 SGB V, hospitals are obliged to operate an internal quality management system and must implement the regulations of the Protection Against Infection Act. Hygiene and Drug Commissions are suitable instruments for this purpose, although they do not yet exist in all hospitals. These Commissions often practice the division of labour, in that the Hygiene Commission particularly deals with epidemiological issues, while the Drug Commission is responsible for structuring drug therapy.

A dialogue between the two Commissions should be ensured to achieve optimum prevention and control of antimicrobial resistances. Cooperation of this kind can, for example, be realised in the framework of an Infection Management Commission: this commission could monitor implementation of the Protection Against Infection Act and the KRINKO recommendations, further develop hygiene regulations, locally implement guidelines for antibiotic therapy and provide advice on the use of antibiotics. To ensure prompt action if resistances emerge locally, the Infection Management Commission could form a Rapid-Response Team, both to serve as a contact point and also to analyse the situation and coordinate the pre-

vention measures in the event of resistances emerging (see also Fig. 1).

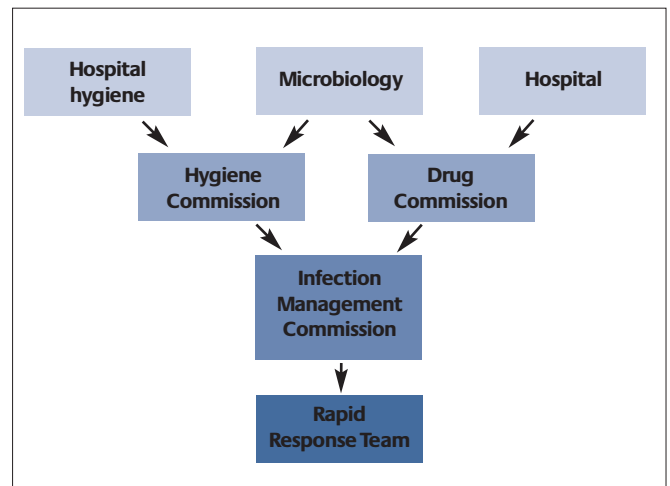


Fig. 1: Possible structure for improving cooperation between organisational units in hospitals

Actions:

- Examination of the possibilities for improving cooperation between responsible organisational units in hospitals

Milestone: Starting in 2009

Participants:

Länder, Länder authorities, Infection Protection Working Group, ÖGD, DKG, G-BA, institution according to Section 137a, hospitals, ÄZQ, KRINKO, German Coalition for Patient Safety, BMG, RKI, scientific societies, KBV

GOAL 4

Safeguarding diagnosis

Requirement:

Improvement of the diagnosis of bacterial infective agents and their antimicrobial resistance in terms of scope, quality and speed

Background:

Pathogen diagnosis that is appropriate to the indication, and also comprehensively includes antimicrobial resistance, makes a major contribution to quality assurance when treating bacterial infections. The application of diagnostic procedures, together with the clinical picture presented by the patients, makes it possible to distinguish between viral and bacterial infections, and also to determine the necessary duration of antibiotic therapy.⁶⁵ This can achieve up to 50% savings on antibiotic prescriptions.²⁴ Additional costs can also be prevented by rapid identification of (multi)resistant infective agents and efficient

(admission) screening of high-risk patients.^{124,125} There is furthermore a need to improve the hospital-wide management and sanitation of patients with multiresistant pathogens in both the inpatient and the outpatient sector.

Test systems for rapid diagnosis can make a supportive contribution in this context, since they allow pathogen diagnosis in a matter of hours. Rapid identification of multiresistant pathogens prevents the further spread of (multi)resistant infective agents, thus promoting targeted antibiotic therapy and the use of narrow-spectrum antibiotics.

General MRSA diagnosis and the decolonisation of MRSA patients are included in the services provided by statutory health insurance. They are taken into account in the framework of the remuneration of SHI-accredited physicians. Beyond this, the SHI system makes no provision for separate remuneration for the use of rapid-diagnosis test systems.

General screening of high-risk patients is not included in the services provided by statutory health insurance and is thus not eligible for reimbursement in the framework of SHI.^{59,65}

The quality of diagnosis is increasingly the subject of criticism.

Actions:

- Review of the eligibility for reimbursement of diagnostic procedures and possible obstacles to their application, as well as identification of deficits and problems in connection with quality assurance in diagnosis

Milestone: Starting in 2009, under the management of the BMG

- Review of the importance of, and preparation of, recommendations for the use of (rapid-test) diagnosis in private practices and hospitals

Milestone: 2009–2010, under the management of scientific societies and experts

Participants:

BMG, RKI, G-BA, SHI, PKV, Regional Associations of SHI-Accredited Physicians, National Association of SHI-Accredited Physicians, IQWiG, committee for rating office-based doctors' services, pharmaceutical industry, ÖGD, hospitals, outpatient practices, rehabilitation facilities and nursing homes, DGHM, BÄMI, veterinary medicine, VDGH

GOAL 5

Promotion of the basic training, specialist training and continuing education of medical occupational groups, pharmacists and natural scientists

Requirement:

Greater emphasis on the subject of antimicrobial resistance in the basic training, specialist training and continuing education of physicians, pharmacists, nursing staff and natural scientists

Background:

Physicians, pharmacists, nursing staff and natural scientists who have knowledge deficits as regards diagnosis, or fail to apply existing knowledge, efficient antibiotic therapy and the avoidance of infections due to resistant infective agents, are also a cause of increasing antimicrobial resistance rates.

The adequate communication of knowledge regarding the antimicrobial resistance problem in the context of basic training, specialist training and continuing education, and application of this knowledge, must be ensured, especially among physicians prescribing antibiotics, but also among pharmacists and hospital nursing staff. Firmly establishing this topic in the basic training, specialist training and continuing education of these occupational groups lays the foundations for appropriate use of antibiotics and appropriate handling of (multi)resistant infective agents. Implementation of the acquired knowledge in practice will contribute to reducing antimicrobial resistance.

The communication between physician and patient also plays an important role in connection with the prescribing of antibiotics. The physician's perception of a patient's wishes has an influence on the prescribing of an antibiotic. However, physicians often do not perceive a patient's wishes correctly. Talking about the patient's needs and the necessity of an antibiotic could counteract the inappropriate prescribing of antibiotics. A supportive contribution in this context can be made by checklists that serve as a basis for discussions between the physician or pharmacist and the patient.

Actions:

- Elaboration of proposals for increasing emphasis on the topics of antimicrobial resistance and patient communication in the basic training, specialist training and continuing education of physicians, pharmacists and nursing staff

Milestone: By mid-2009, under the management of the BMG

- Review of the possibilities for more firmly establishing the subject of antimicrobial resistance in natural science study courses, especially in the study of biology
Milestone: by the end of 2009, under the management of scientific societies, professional associations
- Establishment of a certified continuing education programme for qualification as NIP/ABS Officer (NIP = Nosocomial Infection Prevention, ABS = Antibiotic Stewardship)
Milestone: Initiation in 2009, by DGI and DGHM

Participants:

DGHM, DGI, BMG, BZgA, German Medical Association, German Dental Association, State Chambers of Physicians, State Dental Chambers, Brandenburg State Chamber of Physicians, ABDA, scientific societies, professional associations, universities, patient associations, German Nursing Council

COMPONENT III:

Cooperation and coordination

GOAL 6

National cooperation

Promoting the sustainability of actions and structures in the field of antimicrobial resistance requires content-related and structural cooperation between the Federal Government, the Länder and both public and private players in this field. With the present strategy, an exchange between the players is initiated by the BMG. The recommended structural cooperation and networking of players at the national, Länder and local level is described in the sub-goals below.

Sub-goal 6.1: Cooperation at the regional level

Requirement:

Strengthening of regional cooperation between players in the healthcare sector

Background:

For prevention and control measures for reducing antimicrobial resistances to be successful in the long term, there must be cooperation between the players in the healthcare sector. In this context, cooperation in the various sectors of healthcare should also include cross-sectoral quality assurance pursuant to Section 137 Paras. 1 and 2 and Section 137a SGB V. It has become apparent that the restriction of prevention measures to hospitals alone is insufficient.⁶⁰ For example, an MRSA patient must receive consistent aftercare from the physician in private practice or

the nursing home after being discharged from hospital. In addition, the physician in private practice or the nursing home, and also the patient and his or her relatives, must know what measures are important in the event of infection with a (multi)resistant pathogen. This requires education and training of the staff and/or the relatives.

The establishment of regional networks for prevention and control of MRSA is also recommended at the Länder level (Resolution of the 79th Conference of Ministers Responsible for Health) for containing the growing MRSA problem.

Many of the problems existing as regards the prevention and control of MRSA also occur in connection with other (multi)resistant infective agents. Therefore, the networks recommended by the Conference of Ministers Responsible for Health should not restrict themselves to the MRSA problem.

Regional networks for prevention and control of antimicrobial resistances could be used for discussions, training and continuing education, but also for advising the participating players in the health sector, as well as patients and their relatives.

Interactive meetings offering continuing education, where individual problems and prescribing practices, or local/regional antimicrobial resistance and antibiotic consumption data, are discussed and analysed, promote appropriate antibiotic use by the participating physicians.^{2,32} For this reason, regional networks for the prevention and control of antimicrobial resistances are to be established, based on the model of the MRSA-net EUREGIO project.

The public health service (ÖGD) serves to protect the health of the population and is in permanent contact with all stakeholders in healthcare provision at the regional level. Consequently, the ÖGD should be responsible for the establishment of these regional networks, for the sustainability of the network structure, and also for moderation of the networks.

Actions:

- Pilot projects for creating regional networks for prevention and control of antimicrobial resistances in selected areas
Milestone: By the end of 2009, under the management of the Länder (Infection Protection Working Group) and the ÖGD
- Evaluation of the regional networks and adaptation of the intervention measures following evaluation by the Länder/ÖGD

Milestone: Starting in 2012, evaluation group comprising representatives of the Länder, the ÖGD, universities and the RKI

- Implementation of workshops for network moderators in the public health service

Milestone: 2009; Academy of Public Health and LIGA

Participants:

BMG, RKI, Länder authorities, Infection Protection Working Group, ÖGD, hospitals, (private) microbiological centres/laboratories, outpatient practices, rehabilitation facilities and nursing homes, SHI, PKV, Regional Associations of SHI-Accredited Physicians, National Association of SHI-Accredited Physicians, State Chambers of Physicians, German Medical Association, Scientific Advisory Board of the German Medical Association, Drug Commission of the German Medical Association, scientific societies, professional associations, universities, G-BA, Freiburg Centre for Infectious Diseases, NRC for Surveillance of Nosocomial Infections, Academy of Public Health and LIGA

Sub-goal 6.2: Cooperation at the Federal Government level

Requirement:

Strengthening of interministerial cooperation in the field of antimicrobial resistance

Background:

Antimicrobial resistances occur in human and veterinary medicine, as well as in the environment. The increasing rise in resistance rates and the ubiquitous occurrence of resistances call for a common, interdepartmental strategy for detecting, preventing and controlling antimicrobial resistances in Germany, and also for the coordination of activities for implementing the strategy.

To this end, an Interministerial Working Group for the field of antimicrobial resistance is intended to ensure a dialogue between the players at the Federal Government level. In this Working Group, the competent Federal Ministries will be responsible for interdepartmental coordination of antimicrobial resistance policy in Germany, involving the competent higher federal authorities in the process. The Interministerial Working Group will initially be chaired by the BMG. The goals, tasks and members of the Interministerial Working Group should be defined at a first meeting.

Each department is responsible for coordinating the planning, implementation and controlling of concrete projects and actions in its respective sphere. In addition, interdepartmental projects are also to be planned.

The Interministerial Working Group will also be responsible for interdisciplinary, continuous co-ordination, planning, evaluation, adaptation and expansion of national antimicrobial resistance policy, making it possible to react to new resistance problems. National experts in the field of antimicrobial resistance are to be involved in this context (see also Goal 3).

Actions:

- Establishment of an Interministerial Working Group on Antimicrobial Resistance for interdisciplinary coordination, planning, evaluation, adaptation and expansion of national antimicrobial resistance policy

Milestone: By mid-2008, initiation by the BMG

Participants:

BMG, BMELV, BMBF, BMU, representatives of the respective competent higher federal authorities

Sub-goal 6.3: Coordination of activities at the national level

Requirement:

A coordinating centre for the prevention and control of antimicrobial resistance at the national level

Background:

Numerous activities, projects and recommendations in the field of antimicrobial resistance exist in Germany under very different competences. There has so far been no adequate, top-level, continuous coordination and assessment of these activities. This makes it more difficult to obtain an overview of the resistance situation and coordinate control measures in Germany. Consequently, there is a need to pool, coordinate and assess activities.

Many activities in the field of antimicrobial resistance are already part of the sphere of responsibility of the Robert Koch Institute (see also Goals 1 and 2). As a result of being expanded to take on the role of the national Public Health Institute, the Robert Koch Institute is also becoming increasingly qualified for the central position that it will in future assume at the professional level in the field of antimicrobial resistance in human medicine.

Moreover, the Robert Koch Institute will also provide professional advice at the international, national, regional and local levels. This will include advising the Länder authorities, the public health service and players in regional networks (see also Sub-goal 6.1), as well as advising politicians, expert circles and the public.

Actions:

- Establishment of an agency at the RKI for assessment and advice on the field of antimicrobial resistance,

e.g. a "Centre for Prevention and Control of Antimicrobial Resistance"

Milestone: By the end of 2008, under the management of the RKI

Participants:

BMG, RKI, Länder, scientific societies

GOAL 7

International cooperation

Requirement:

Promotion of international cooperation and strengthening of Germany's position in international networks

Background:

International cooperation, particularly with the European Centre for Disease Prevention and Control (ECDC), will be strengthened by implementing the strategy. The exchange of information and data with European and international partners permits an assessment of the resistance situation in Germany and can indicate new solution approaches and prospects for reducing antimicrobial resistance.

International cooperation is particularly necessary in connection with the containment of infectious diseases and antimicrobial resistances, since the transmission of (resistant) pathogens will continue to rise as a result of growing globalisation and the increasing mobility of the population.

Moreover, antimicrobial resistance is a high-priority topic for the ECDC. Some of the activities planned by the ECDC in the field of antimicrobial resistance go hand-in-hand with activities within the strategy. This offers Germany the opportunity to actively participate in European activities, voice German interests and advance the control and avoidance of antimicrobial resistance at the global level.

Implementation of the strategy also aims to strengthen Germany's position in international networks. At the same time, the principal goals formulated in the Recommendation of the European Commission on the prudent use of antimicrobial agents in human medicine (2002/77/EC) are actively implemented.

Actions:

- Strengthening of German participation in international projects and networks, e.g. EARSS and ESAC

Milestone: By the end of 2010, under the management of the RKI

Participants:

BMG, RKI, scientific societies

COMPONENT IV:

Research and evaluation

GOAL 8

Promotion of evaluation measures in human medicine

Requirement:

Evaluation of measures for controlling and minimising antimicrobial resistance

Background:

Numerous intervention measures can be introduced in order to promote the appropriate use of antibiotics and reduce antimicrobial resistance rates.^{2,32} Only additional studies can determine whether intervention measures, e.g. new treatment measures, are effective. This requires an analysis of the actual situation in advance and evaluation following introduction of the intervention measure.^{23,25}

In the framework of the present strategy, an initial analysis is to examine the factors influencing antibiotic prescribing practices and (previously) successful interventions for promoting the efficient use of antibiotics in human medicine.

Rising resistance rates, increasing consumption of broad-spectrum antibiotics and major regional differences in antibiotic consumption in Germany suggest that physicians occasionally prescribe antibiotics inappropriately. Next to no information is available on the factors governing the practices of physicians in outpatient and inpatient care in Germany, or on how relevant these factors are. However, to be able to introduce targeted interventions for reducing antibiotic consumption in Germany, there is first a need to know the influencing factors that lead to antibiotics being prescribed, and also their individual relevance.

Therefore, the following questions are to be investigated in a study:

- Which factors influence physicians in Germany when prescribing antibiotics?
- What is the relevance of these influencing factors when prescribing antibiotics?
- What instruments or measures are suitable for promoting appropriate prescribing of antibiotics and thus counteracting the increasing development of resistances?

In addition, the application by physicians of diagnostic (rapid-test) methods, and of recommendations and

guidelines for antibiotic therapy, is to be surveyed, as well as their benefits as regards the prescribing of antibiotics (see also Goals 3 and 4).

The results of the study will permit characterisation of the influencing factors, and targeted intervention measures can then be introduced on this basis.

Moreover, patients are to be asked about the correct intake of antibiotics, their expectations of physicians regarding the prescribing of antibiotics, and their knowledge in this field. If appropriate, the results of this survey are subsequently to be used as a basis for implementing a targeted education campaign for the general public. This could achieve substantial savings, both in individual medical institutions and in the health system as a whole.

The strategy, and the projects and actions it contains, are simultaneously to be evaluated by the ECDC. The ECDC has past experience with evaluating the EU Member States in the field of antimicrobial resistance. A study of the actual situation in the field of antimicrobial resistance in Germany was already performed by the ECDC in October 2007.

Actions:

- Study of the antibiotic prescribing practices of physicians in Germany (funding has already started)
Milestone: By the end of 2008, under the management of the RKI
- Survey of patients on the correct intake of antibiotics and their expectations of physicians when it comes to prescribing antibiotics
Milestone: By the end of 2009, under the management of the RKI
- Evaluation of the national Antimicrobial Resistance Strategy
Milestone: Ongoing, under the management of the ECDC
- Adaptation of the German Antimicrobial Resistance Strategy
Milestone: Ongoing, under the management of the BMG

Participants:

BMG, RKI, State Chambers of Physicians, German Medical Association, Brandenburg State Chamber of Physicians, outpatient and inpatient physicians prescribing antibiotics, SHI, PKV, Regional Associations of SHI-Accredited Physicians, National Association of SHI-Accredited Physicians, scientific societies, professional associations, ECDC, KRINKO

GOAL 9

Promotion of knowledge transfer in the field of antimicrobial resistance

Requirement:

Strengthening of knowledge transfer between antimicrobial resistance research, practice and the public

Background:

The possibility of creating an Internet-based platform on antimicrobial resistance for physicians and medical occupational groups is being examined to promote the appropriate use of antibiotics. In addition to information on infections, the action of antibiotics, resistance development and new antibiotics, the site could also be used to publish generally acknowledged recommendations and guidelines for antibiotic therapy (see also Goal 3) and significant research results relating to antimicrobial resistance. Experts and professional circles would have rapid access to new, practice-relevant measures and/or guidelines in the field of antimicrobial resistance. An Internet-based platform permits a rapid exchange of information and up-to-date information at all times. To increase knowledge transfer between research and everyday clinical or practice work, it would also be possible to compile and assess current and significant research results or information on the efficacy of new substances in one area of the platform. Consequently, the first step should be to determine the need for a platform of this kind (see Goal 8).

In addition, education and information of the general public in the field of antimicrobial resistance can also promote the correct intake of antibiotics and thus contribute to the fight against antimicrobial resistance.

Actions:

- Examination of the need for, and feasibility of, an Internet-based platform on antimicrobial resistance
Milestone: By the end of 2009, under the management of the RKI
- Development of an information sheet on the safe use of antibiotics, and expansion of the information on common illnesses in the cold months for which antibiotics are used, in the framework of the Health Information for the Public
Milestone: By the end of 2008, IQWiG
- Recommendation on use of the Health Information for the Public of the IQWiG by health insurance funds to educate and inform insureds
Milestone: Starting in 2009, SHI
- Provision of specific information offerings for SHI-accredited physicians, e.g. in the context of quality circle work
Milestone: Starting in 2009, KBV

- Target group-oriented selection, preparation and forwarding of information in the field of antimicrobial resistance

Milestone: Starting in 2009, BÄK and LÄK

- Review of the possibility of, and need for, further education and information for the public

Milestone: Starting in 2009, under the management of the BMG

Participants:

BMG, RKI, scientific societies, State Chambers of Physicians, German Medical Association, SHI, PKV, Regional Associations of SHI-Accredited Physicians, National Association of SHI-Accredited Physicians, IQWiG, BZgA

GOAL 10

Networking and strengthening of science in the field of antimicrobial resistance

Requirement:

Analysis of the need for research into antimicrobial resistance

Background:

Containing resistances will be an important task in the years to come. The subject of antimicrobial resistance is already being dealt with in various measures of the BMBF. However, there is a need for coordinated activity for networking that, for example, also closes the gap between research on the development of antimicrobial resistance, the spread of resistances and the measures for containing resistances.

Actions:

- Determination of deficits and problems in research in the field of antimicrobial resistance in Germany

Milestone: By the end of 2009, under the management of the BMBF

Participants:

BMBF, BMG, BMELV, BMU, science, industry



6 DART in the field of animal husbandry, the food chain and veterinary activity

6.1 Existing measures for minimising antimicrobial resistance

The significance for human health described above already led in the past to the introduction of a number of measures for minimising antimicrobial resistances in the field of animal husbandry, the food chain and veterinary activity. Specifications of the European Community and supranational specifications (WHO/FAO/Codex Alimentarius) were taken into account and implemented in the context of these measures.

Measures aimed at minimising the occurrence of antimicrobial resistance must be scientifically sound and give consideration to the need for effective antibiotics in animal healthcare to restore the health of animals. One aim of the measures for minimising antimicrobial resistances in veterinary medicine is to ensure the protection of consumer health. In this spirit, measures also have to be taken in the framework of preventive consumer protection if risk assessment indicates their necessity in individual instances. The measures taken in such a case have to be scientifically verified.

Similarly, the measures to be taken must be capable of effectively fulfilling specifications concerning the handling of antimicrobial resistances in animals that affect international trade (OIE, WHO/FAO/Codex Alimentarius).

6.1.1 Measures in Germany

The measures taken to date, or currently being implemented, are attributable, inter alia, to two international symposia, held in 2003 and 2004 at the Federal Institute for Risk Assessment (BfR) and the Federal Office for Consumer Protection and Food Safety (BVL) on risk assessment and the minimisation of antimicrobial resistance in the sense of a risk management measure. In addition, the German Veterinary Association established measures in Germany as long ago as 2000, e.g. the Guidelines for prudent use of antimicrobial agents in veterinary medicine (Antibiotic Guidelines). In the scientific sector, the subject of resistance is dealt with in the former BGVV (now BfR and BVL) and, for more than 20 years and with international standing, formerly in the Federal Agricultural Research Centre (FAL) and now at the Friedrich Loeffler Institute (FLI), all in the portfolio of the BMELV. Among other things, this has resulted in recommendations for action for veterinary practice, also in cooperation with the German Society for Veterinary Medicine (DVG).

All antibiotics for veterinary medicine are available on prescription only.

So-called antibiotic performance promoters^{a)} in animal feed have been banned throughout Europe since 2006. Various performance promoters have been successively banned in the Community since 2000, or are no longer used for lack of acceptance among consumers. As a result, overall antibiotic consumption in the field of animal husbandry has declined in Germany. At present, however, only estimates²¹ are available in Germany regarding the sales figures for antibiotics, but they nevertheless permit conclusions to be drawn about the significance and market shares of certain antibiotics.

The following measures have essentially been completed: elaboration of Antibiotic Guidelines (Federal Chamber of Veterinaries), implementation of continuing education measures, restriction of the sale of systemic antibiotics and ban on farm mixes by the 11th AMG Amendment,

a) Enterically non-absorbable antibiotics that were allowed to be added to the feed of certain farm animals as EC-approved feed additives for improving fattening performance and stabilising intestinal health.

b) This Ordinance applies to businesses that keep food-producing animals.

restriction of the indications for antibiotics of particular therapeutic importance in human medicine, recommendations on standard in-vitro susceptibility testing (preparation of antibiograms) for certain infective agents in animals, demand for resistance data when applying for registration and re-registration of antibiotics.

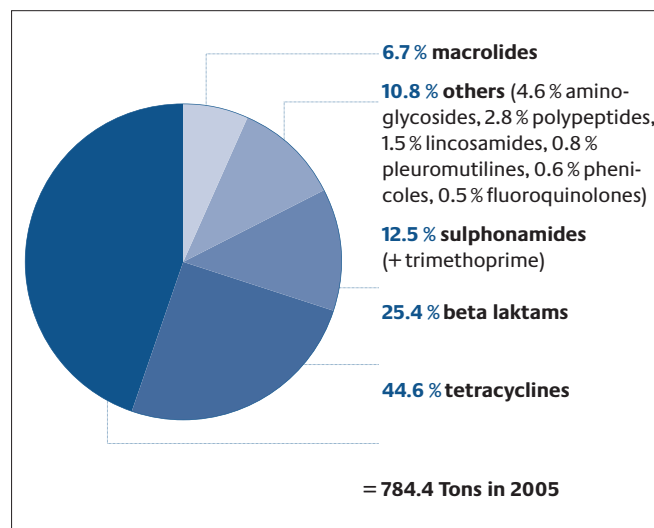


Fig. 2 Sales figures for antibiotics in veterinary medicine in Germany²¹

6.1.1.1 Legal bases

The German Drug Law (AMG) regulates transactions involving medicinal products, including veterinary medicinal products, but excluding veterinary vaccines. Among other things, the AMG contains the fundamental specifications for the registration, production, sale and use of veterinary medicinal products, including antibiotics. The following are some of the additional regulations applicable to antibiotics:

- Mandatory Prescription of Medicinal Products Ordinance (AMVV, regulates the mandatory prescription of antibiotics, etc.)
- Ordinance on the Specification of Requirements for the Application for Marketing Authorisation, Prolongation of the Authorisation and Registration of Medicinal Products
- German Drug Law Documentation Submission Ordinance
- Ordinance on the Documentation Obligations of Animal Owners for Medicinal Products Intended for Use in Animals^{b)}
- Ordinance on the Electronic Notification of Side Effects
- General Administrative Regulation on the Surveillance, Collection and Evaluation of Drug Risks (Graduated Plan) according to Section 63 German Drug Law

- Veterinary House Dispensary Ordinance (TÄHAV)
- Certificate Accompanying Medicated Foodstuffs according to Section 56 Para. 1 AMG
- General Administrative Regulation on the Application of Medicinal Product Testing Guidelines for Veterinary Medicinal Products

The German Drug Law and the implementing regulations enact the specifications of European law in Germany. The registration of veterinary medicinal products in Germany is based on the specifications envisaged in Community law.

As a general rule, there is a ban on treatment of certain epizootic diseases (e.g. brucellosis) under Germany's Epizootic Diseases Act, and a ban on treatment of salmonella-infected poultry flocks exists under Regulation (EC) No. 1177/2006.⁴²

In addition, food law serves as a basis for implementing studies on the occurrence of antimicrobial resistance in zoonotic agents or pathogens of importance for human health in the food chain. The studies range from the living animal to trade in foods of animal origin (General Administrative Regulation on Zoonoses in the Food Chain).

6.1.1.2 Monitoring

In Germany, the Länder are responsible for monitoring the regulations of drug law, epizootic disease law and food law. The Federal Government provides facilities for harmonising and standardising methods and investigations (e.g. reference laboratories), as well as for pooling and assessing results.

6.1.1.2.1 National Reference Laboratory for Antimicrobial Resistance

A National Reference Laboratory for Antimicrobial Resistance (NRL Antimicrobial Resistance) has been established at the Federal Institute for Risk Assessment (BfR) in Germany in the framework of the specifications of Regulation (EC) No. 882/2004⁴³. The laboratory performs the tasks specified in Article 33 of Regulation (EC) No. 882/2004. The National Reference Laboratory is particularly intended to contribute to achieving high quality and consistency of the results of studies on zoonotic agents. The work focuses on collecting comparable data on antimicrobial resistance for zoonotic agents and other pathogens, insofar as they pose a threat to public health. To this end, the NRL Antimicrobial Resistance coordinates selection of the isolates to be tested from the food chain with the Länder and their testing institutions, also itself performing resistance testing on isolates originating from animals, foodstuffs and feedstuffs, and from the environment. Testing

for resistances is performed on a routine basis, using internationally acknowledged, quantitative methods in an accredited laboratory unit. The quality of the results is ensured by participation in international interlaboratory tests (e.g. at the Community Reference Laboratory (CRL) for Antimicrobial Resistance). Numerous modern methods of molecular biology are used for targeted epidemiological testing of resistances, their molecular bases, transmission and spread. The NRL engages in intensive cooperation with the CRL for Antimicrobial Resistance to this end. Standardisation of the tests for antimicrobial resistance is a prerequisite for consistent monitoring of the occurrence of resistances. It permits data exchange and comparison at the national and international level. In this context, the methods based on the specifications of food law, including the cut-off values, so far differ from the recommendations for testing clinical cases.

6.1.1.2.2 Monitoring and testing of pathogens of importance for human health

In the framework of Directive 2003/99/EC⁴⁷, the Member States are to collect data on the prevalence of zoonoses and zoonotic agents and their antimicrobial resistances in animals, foodstuffs, feedstuffs and humans, in order to obtain information on the development trends and sources of zoonoses and the resistance situation. These data are compiled by the Länder and the municipalities, then being pooled centrally and assessed nationally. Above and beyond this, the data are also evaluated by the European Food Safety Authority (EFSA). Article 7 of the Directive forms the legal basis for further measures to be implemented in the Community. Attention currently focuses on monitoring Salmonella in poultry and Campylobacter in poultry in the framework of limited-period studies (Decision 2007/516/EC⁴⁴). Decision 2007/407/EC⁴³ has committed Germany to monitor the antimicrobial resistances of Salmonella in poultry and pigs in the framework of the basic studies since 2007 (turkeys and fattening pigs) and the programmes for controlling Salmonella in these animals that have to be implemented in accordance with Regulation (EC) No. 2160/2003⁴⁸ and its associated Regulations. Moreover, the prevalence and resistance attributes of methicillin-resistant Staphylococcus aureus (MRSA) are being monitored in a study on breeding pigs, which is also being expanded by the Länder on a voluntary basis to include available fattening holdings in the framework of the study (Decision 2008/55/EC⁴⁵). In this context, the task of the NRL Antimicrobial Resistance is to coordinate the studies and measures, and to provide the competent laboratories of the Länder with method recommendations. The nationwide implementation of the survey of antimicrobial resistance,

and of Decision 2007/407/EC, is regulated by the provisions of the General Administrative Regulations on the Recording, Evaluation and Publication of Data on the Occurrence of Zoonoses and Zoonotic Agents in the Food Chain (General Administrative Regulation on Zoonoses in the Food Chain, Federal Gazette 106, p. 2587). The BfR can propose additional measures in this framework, also for other zoonotic agents. MRSA is to be taken into consideration in the sampling plan for zoonosis monitoring from 2009 to 2011 on the basis of this General Administrative Regulation on Zoonoses in the Food Chain.

6.1.1.2.3 Monitoring of resistance in zoonotic agents

Since 2001, the BVL has been conducting a continuous, annual data collection and investigation regarding the susceptibility of clinical bacterial isolates (GERM-Vet programme) to selected antibacterial agents. The data are collected according to a detailed, statistically proven sampling plan that is modified annually in keeping with the current situation. Since the 2006/2007 study, the range of bacteria covered has been expanded to include isolates from diseased non-food-producing animals. The bacterial isolates are sent in by state (Länder) and private laboratories, and epidemiological parameters (e.g. data on herd size, type of use, type of housing, animal age and sampling date) are collected at the same time. The regional share of the number of bacterial strains per species is calculated on the basis of the total livestock figures for the individual Länder. The data are recorded and communicated by means of a web-based database. The minimum inhibitory concentration is determined and assessed (method: bouillon microdilution) at the BVL according to the CLSI^{c)} standard. In addition to establishing the current resistance situation, this also permits early detection of a change in the resistance situation in Germany. All isolates are preserved in a master collection.

A monitoring programme complementary to the GERM-Vet programme was carried out in Germany under the name BfT-GERM-Vet in the period 2004 to 2006^{d)}. The BfT-GERM-Vet study was implemented by a consortium comprising scientists from the Friedrich Loeffler Institute (FLI), the Free University of Berlin, the Ludwig Maximilian University of Munich and the Federal Office for Consumer Protection and Food Safety (BVL). This study examined pathogens from a total of 31 bacteria/animal/disease process combinations regarding their susceptibility to 24 antimicrobial active substances and active substance

combinations. In contrast to GERM-Vet, the BfT-GERM-Vet study focused on bacterial infective agents of the animal species dog, cat and horse. Bacteria from cattle and pigs were additionally examined that originated from disease processes not included in the studies of the GERM-Vet programme. BfT-GERM-Vet and GERM-Vet adhered to the same sample collection plan and used the same CLSI method for susceptibility testing by means of bouillon microdilution and for assessing the results obtained. Moreover, the bacterial isolates for both studies, BfT-GERM-Vet and GERM-Vet, were provided by largely the same diagnostic institutions of the Länder and veterinary medical training institutions, as well as the same private diagnostic laboratories. The complete results of the BfT-GERM-Vet study, and selected results of GERM-Vet, were published in a special issue of *Berliner und Münchener Tierärztliche Wochenschrift* in autumn 2007.

Together with the Paul Ehrlich Society (PEG) and with the involvement of experts, the BVL is, as a member of the coordination group, currently compiling an “Atlas of Antimicrobial Resistance and Antibiotic Consumption in Germany”, which will incorporate both consumption and resistance data from human medicine and resistance data from the GERM-Vet programme and the BfT-GERM-Vet project. The Resistance Atlas was presented to the public at a press conference in the framework of the annual conference of the PEG in October 2008.

6.1.1.2.4 Active substance-specific monitoring studies

Using the CLSI method for susceptibility testing by means of bouillon microdilution, the Institute of Farm Animal Genetics of the Friedrich Loeffler Institute (FLI) performed, from 2000 to 2007, continuous monitoring of bovine (*Pasteurella multocida*, *Manheimia haemolytica*) and porcine (*Pasteurella multocida*, *Actinobacillus pleuropneumoniae*, *Streptococcus suis*, *Bordetella bronchiseptica*) respiratory infective agents regarding their resistance to florfenicol. Monitoring of coagulase-negative staphylococci from cases of subclinical mastitis in dairy cows for susceptibility to pirlimycin and reference substances was additionally performed from 2004 to 2006.

Both studies represent investigations into the resistance development of pathogens relevant in veterinary medicine to antimicrobial active substances that have only been used therapeutically in veterinary medicine for a relatively short time. The molecular studies carried out parallel to these two monitoring studies on the underlying resistance genes and mechanisms in resistant isolates constitute an important component with respect to a “hazard identification” in the framework of a risk analysis.

c) Clinical and Laboratory Standards Institute
d) A voluntary initiative of the BfT

6.1.1.3 Registration and pharmacovigilance for antibiotics for veterinary medicine

The registration of antibiotics for veterinary medicine, and also supervision of the products following registration, is managed by the Federal Office for Consumer Protection and Food Safety (BVL). As a general rule, all antibiotics registered for use in veterinary medicine are subject to mandatory prescription.

6.1.1.3.1 Registration requirements for antibiotics for veterinary medicine

The BVL examines registration applications and decides on the registration of antibiotics on the basis of the EU law implemented in the AMG, also giving consideration to relevant EU Guidelines^{29,51} for national applications.

In principle, the same registration requirements exist for both known and new substances. As regards the resistance problem, information particularly has to be submitted concerning the fields of pharmacokinetics, pharmacodynamics, toxicology, ecotoxicology, the residue situation and clinical aspects. Among other things, the applicant must, for example, investigate and demonstrate the degradation path of substances with antimicrobial activity.

To demonstrate the susceptibility of claimed target pathogens, the applicant is required to submit representative MIC (minimum inhibitory concentration)^{e)} values from the past five years. Moreover, comprehensive data have to be provided regarding resistance (development, mechanisms, cross and co-resistance).⁵¹ Furthermore, when registering antibiotics for food-producing animals, additional data have to be submitted regarding susceptibility and resistance, also in relation to the resistance risk for humans. The data to be provided in this context refer to zoonotic agents and commensal organisms (salmonellae, *Campylobacter*, enterococci and *E. coli*)²⁹. The expert information and instructions for use include standard notes for the veterinary, agreed on at the EU level, that are intended to promote prudent use of medicinal products of this kind. For instance, the standard sentence "... should only be used after preparation of an antibiogram" is nowadays required for all antibiotics.

If the resistance situation is unclear, the BVL makes use of its powers to impose conditions in the context of registration, e.g. in the form of a Post-Marketing Monitoring programme.

6.1.1.3.2 Pharmacovigilance

The World Health Organization (WHO) defines pharmacovigilance as all activities concerning the discovery, assessment, understanding and prevention of side effects or other problems relating to medicinal products. According to Section 63b AMG, the pharmaceutical manufacturer is obliged to collect and assess reports from users and official agencies concerning veterinary medicinal products, and to take suitable action for averting risks, where appropriate. The competent higher federal authorities are to be informed accordingly. To prevent threats to human and animal health, the competent registration authorities are required to centrally record and evaluate the risks occurring when using veterinary medicinal products, especially side effects, interactions with other agents, adulteration and potential risks for the environment resulting from use of a veterinary medicinal product, and to coordinate the measures to be taken according to the AMG (Section 62 AMG).

The details are regulated by the General Administrative Regulation on the Graduated Plan. According to Article 1 No. 3 of this General Administrative Regulation, the development of resistance to anti-infective agents is one of the drug risks to be monitored, collected and evaluated.

Above and beyond the registration approval, pharmaceutical manufacturers are fundamentally obliged to monitor the efficacy and resistance development of the respective antibiotic in the framework of pharmacovigilance. Regular reports are to be submitted and, if necessary, the registration adapted by means of amendment procedures in keeping with the new findings.

6.1.1.4 Regulations on the sale of antibiotics for systemic use

As a general rule, the veterinary surgeon himself administers antibiotics to animals – in direct connection with examination and diagnosis. However, antibiotics are also sold to animal owners for continuing therapy or for group treatment.

The AMG contains specific regulations concerning the sale of antibiotics for systemic use in food-producing animals to animal owners by veterinary surgeons. As for all pharmacy-only veterinary medicinal products, systemic antibiotics may as a general rule only be sold for animals

e) The minimum inhibitory concentration (MIC) is the smallest active substance concentration of an antimicrobial substance (e.g. of an antibiotic) that still prevents pathogen multiplication in culture.

treated by the veterinary surgeon. The details are regulated in Section 12 of the Veterinary House Dispensary Ordinance (TÄHAV, Federal Law Gazette I, p. 3455, 2006). Additionally, antibiotics for systemic use in the treatment of food-producing animals may only be sold in quantities sufficient for a maximum of seven days ("7-day regulation" according to Section 56a AMG). Exceptions are antibiotics for which therapy lasting longer than seven days is expressly specified according to the registration documents. This regulation is intended to help ensure that antibiotics are only used immediately around the time of diagnosis.

6.1.1.4.1 Recording of the quantities of antibiotics sold

To assess the development and spread of antimicrobial resistance, there is a need to record the quantities of antibiotics sold. This makes it possible to identify and evaluate possible links between the quantities of antibiotics used and developments in the field of antimicrobial resistance, so that the information obtained can be taken into consideration in risk assessment and risk management. Section 47 Para. 1c of the German Drug Law (AMG) therefore contains the legal basis for recording the quantities of antibiotics sold, which is currently being elaborated. There is a need to be able to establish a regional connection between the quantities of the respective antibiotic sold and regional resistance data for assessment of the resistance risk.

In addition to the quantities of antibiotics sold, an appropriate assessment should also take into account further data, especially data broken down by region concerning the use of antibiotics in food-producing animals, the nature of the livestock holdings, holding structures, including the size of the holdings, and the infection situation in the period under review.

6.1.1.4.2 Recording of the quantities of antibiotics used

Any use of antibiotics in veterinary medicine creates the possibility of selection of antimicrobial resistances in bacteria occurring in animals. A relationship has been described between the use of antibiotics in veterinary medicine and the development of resistances in humans. The quantity of antibiotics used is an important influencing variable that must be taken into account when considering the phenomenon of antimicrobial resistance as a whole. The combined basis of consumption quantities and epidemiological data makes it possible to examine the correlation existing between the quantity of antibiotics used and the development and spread of antimicrobial resistance. Statements regarding the quantities of

antibiotics consumed are therefore also significant for assessing the question of whether these antibiotics pose a threat for humans or animals.

The currently valid regulations of drug law only permit recording of the quantity of antimicrobial agents sold to veterinary surgeons by pharmaceutical manufacturers (Section 47 Para. 1c German Drug Law, see Chapter 6.1.1.4.1).

On the occasion of the international symposium "Risk Management for Containing Antimicrobial Resistance", held at the BfR in late 2004, a call was made for detailed recording of consumption quantities as a risk management measure, and for creation of the necessary statutory basis.

A project being implemented by the BfR on behalf of the BMELV is therefore examining what method could be used for representative recording of consumption quantities on the basis of existing, prescribed records of treatments performed on animals and sales of veterinary medicinal products to animal owners. Particularly important in this context is the question of representative data recording in veterinary practices and livestock businesses, as well as the question of processing these data and forwarding them to the competent higher federal authorities. As a result of the project, it is to be possible to present framework criteria for the legal regulation of the recording of consumption quantities.

Should the research project prove capable of developing a method that can be used nationwide for the representative recording of consumption quantities, the possibility must be examined of introducing regulations in drug law on compulsory recording of the quantities of antibiotics used in food-producing animals. The data then resulting from the recording of consumption quantities are to be suitable for use for permanent risk assessment of antimicrobial resistance development by the higher federal authorities.

The project is specifically intended to examine technically feasible ways of recording the quantities of antibiotics consumed. To this end, a model is first to be developed for statistically representative recording of the quantities of antibiotics used in food-producing animals by evaluating the information in the stock records of animal owners and in usage and sales records of veterinary surgeons. The data recording method developed will be tested in a field trial to determine whether/how and at what expense consumption quantities can be recorded nationwide in Ger-

many.

Up to now, data on consumption quantities are available only in published surveys by Hanover University of Veterinary Medicine in collaboration with the supervisory authorities in Schleswig-Holstein from 2002 and 2003⁷⁻¹¹ and in a doctoral thesis from the University of Leipzig on the development of the use of antimicrobially active veterinary medicinal products in medicated foodstuffs⁹³.

6.1.1.5 Antibiotic Guidelines

Since November 2000, the German Veterinary Association and the former Working Group of Senior Veterinary Inspectors (ArgeVet) have, with the involvement of the affected interest groups and the Federal Ministries, established "Guidelines for the prudent use of antimicrobially active veterinary medicinal products". These Antibiotic Guidelines are currently being amended to reflect the latest scientific knowledge and the conditions prevailing in practice, in order to ensure that they give veterinary surgeons a dependable guide enabling the safe use of antibiotics and safeguarding animal health. These Guidelines set forth the principles for treating animals with antibiotics (not only for food-producing animals). They present the rules of veterinary medical science for the use of antibiotics that must be observed in any correct treatment according to Sections 1a and 12 of the Veterinary House Dispensary Ordinance (TÄHAV, Federal Law Gazette I, No. 66, p. 3455). For example, these Guidelines define the framework for the use of antibiotics in metaphylaxis and therapy. Similarly, the veterinary surgeon is called upon to review the efficacy of his therapy and to prepare an antibiogram when changing antibiotics in order to critically appraise the use of the antibiotic.

6.1.1.6 Use of antibiotically active substances in food production

A further aspect is the use of antibiotically active substances in food production. For reasons of preventive consumer protection, antibiotically active substances, especially substances also used in human medicine, are only to be used in foods on an extremely restrictive basis and not beyond the sphere approved to date.

In food production, the use of natamycin (synonym: pimaricin) as a food additive is approved for treating the surface of various types of hard cheese, as well as dried and salted meats/sausages. In this context, the natamycin content may not exceed 1 mg/dm² surface area, and the substance may not be detectable 5 mm below the surface.

In human medicine, natamycin is used as an antimycotic for topical treatment of yeast infections of the intestine and mycotic infections of the mouth, eyes, eyelids and lacrimal ducts. It is not absorbed in the intestines.

As generally envisaged by the procedure for registering food additives at the level of Community law, and also at the international level (Codex Alimentarius), natamycin was also assessed by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) on several occasions (1968, 1976, 2002, 2003), and by the Scientific Committee on Food (SCF) of the EU Commission in 1979, as regards the safety, in terms of health, of use in foods, specifically against the backdrop of the issue of possible antimicrobial resistance. In this context, general-purpose use in or on foods was considered to be unacceptable, whereas the use of natamycin for treating the surface of the rind of semi-hard cheese matured under aerobic conditions, and for treating the surface of the skin of specific types of sausage requiring a certain maturing process prior to marketing, was accepted on the following conditions:

- Only the end product is treated with natamycin,
- At the time of sale, the natamycin residues on the foods, expressed in relation to the surface of the sausage skin or cheese rind, may not exceed 1 mg/dm² and not be detectable 5 mm below the surface.

Moreover, the SCF – and also the BfR – expressed strict opposition to any more extensive use of natamycin, e.g. for treating the surface of ham, wine and other beverages. These requirements of the SCF were taken into account when registering natamycin in the entire EU (see above).

In a statement issued in 2003, the BfR additionally pointed out that consumers should be advised to remove cheese rinds or the outer layer of cheese that does not have a typical cheese rind or on which no rind is to be seen. This is aimed to counteract the danger of consumers unintentionally taking in small quantities of natamycin, as a result of which the microflora of the intestinal tract could be affected and resistances could occur.

The Commission of the European Communities, and the Committee on Consumer Affairs, Public Health and Consumer Policy of the European Parliament, advocated that antibiotics used in human medicine be employed only restrictively in foods.

6.1.1.7 Use of streptomycin against fire blight in pomaceous fruit

Fire blight is a bacterial disease (pathogenic agent: *Erwinia amylovora*) that can cause severe losses, especially in pomaceous fruit (apples, pears, quinces). Of the approx. 40,000 hectares (ha) of pomaceous fruit (dwarf fruit tree orchards) in Germany, the growing regions in the southern Länder currently face the greatest risk for climatic reasons. Baden-Württemberg is particularly hard-hit, with approx. 11,000 ha apple and pear orchards, including approx. 7,200 ha in the Lake Constance area alone. Should climate change progress, the severely affected areas will grow. Since 1993, there have been financial losses due to fire blight in many Länder, including uprooting of severely affected orchards. 2007 was a particularly bad year for the disease.

Although trade journals repeatedly offer new control methods and a number of plant protection agents and plant strengtheners are available, it has so far not been possible to find a substitute for the use of plant protection agents containing antibiotics that offers the necessary degree of reliability. Nonetheless, it continues to be a demand widely supported in society as a whole that the use of antibiotics be restricted as extensively as possible for reasons of consumer protection.

6.1.1.7.1 First strategy from 2003

A first strategy, geared to a five-year period, was adopted in 2003 with the support of all affected authorities at the Federal and Länder level, as well as of the affected associations in the fields of fruit-growing, bee-keeping, consumer protection, environmental protection and nature conservation. This strategy was generally rated as a success by all concerned, but it has still not proved possible to achieve the goal of ultimately dispensing with the use of plant protection agents containing antibiotics. It was therefore agreed that the “Strategy for Controlling Fire Blight in Fruit-Growing without Antibiotics” should be updated and pursued for a further five years, but with continuing annual reviews. The aim of the Strategy for Controlling Fire Blight in Fruit-Growing without Antibiotics is to comprehensively and specifically fulfil the demands of society as a whole. This strategy paper first provides an in-depth review of the situation in fire blight research, developments and the currently available control options. Both the possibilities existing in the framework of the cultivation methods and direct control methods are discussed. Each descriptive section ends with an assessment by the experts involved in developing the Strategy for Controlling Fire Blight in Fruit-Growing without Antibiotics.

6.1.1.7.2 Orderly termination of the use of antibiotics

Following exhaustive discussions, the conclusion was

drawn that a need for orderly termination of the use of antibiotics to control fire blight results from the assessment of possible residual risks and the concept of preventive consumer protection. It can be assumed that society as a whole will only be willing to accept the use of plant protection agents containing antibiotics for a limited time to come. All the action taken to date is currently insufficient for reducing the risk of infection with fire blight to such an extent that the use of plant protection agents containing streptomycin can be completely abandoned. Given this background and the existing efforts to establish effective alternatives to controlling the agent causing fire blight with plant protection agents containing antibiotics, the strategy is to approve the use of plant protection agents containing streptomycin on a short-term basis and only in cases where it is absolutely necessary, although the ultimate objective is to dispense completely with the use of plant protection agents containing antibiotics.

A comprehensive strategy for controlling fire blight without antibiotics must take the following aspects into consideration, in particular:

- By taking suitable measures, the predisposition of the fruit trees should be reduced to such an extent that only an unavoidable risk of infection remains.
- All the available preventive measures and procedures should be exhausted.
- Direct plant protection measures for controlling fire blight (use of plant protection agents) are only to be taken if this is unavoidable, despite all cultivation-related measures.
- The regulations of the Fire Blight Ordinance should be reviewed and enforced by the Länder consistently and as uniformly as possible.
- The separately elaborated strategy for controlling fire blight, geared to ecological farming, is to be further developed.
- All measures included in the strategy must enable beekeepers and fruit-growers to continue to produce honey and fruit economically.
- The level of protection required in valid food and plant protection law must be observed without fail, especially with a view to preventive consumer protection.

The catalogue of measures that follows covers a very broad approach. It encompasses measures in the fields of plant cultivation and plant protection methods, plant breeding, research, plant protection agents and plant strengtheners, stone fruits, bee-keeping, possibilities for

problem containment, adaptation of the Fire Blight Ordinance, ecological farming, public relations work and marketing. The official agencies or associations involved are responsible for realising the measures. Regarding approval by the BVL of the putting into circulation and use of plant protection agents containing streptomycin, which is part of the measures, the strategy paper already sets out a very narrow framework that is also linked to a number of fundamental prerequisites.

- Ecological fruit-growing, and the applicable special requirements, are likewise taken into account in this strategy. Details are given in a separate strategy that needs to be developed further.
- The Fruit-Growing Expert Group of the Federal Committee for Fruit and Vegetables, and the affected Länder, agree to submit to the BMELV, by 1 October each year, a report on the fire blight situation, the results of honey monitoring and the fire blight prevention measures taken in the framework of the strategy.
- Based on these reports and other new information, a supervising working group compiles an overall report that is discussed with the affected Federal Ministries, the Länder and the affected associations.

6.1.1.8 Sensitisation and education

To sensitise animal owners and veterinary surgeons regarding the subject of antimicrobial resistance, it would appear sensible to use events and continuing education opportunities as a way of communicating, to as many people as possible, a basic knowledge in matters of antibiotic use and the resultant development of resistances, as well as the latest detailed knowledge on various antibiotics and the associated resistance phenomena. This includes basic and specialist training, but also the public portrayal and advertising of antibiotics. Consequently, highly diverse events are offered at many levels in order to draw attention to the significance and background of antimicrobial resistance.

6.1.1.8.1 Risk communication

Annual reports – which are also freely available on the Internet – on the current resistance situation and on development trends are an important element of risk communication. This is defined as a continuous and interactive process and is characterised by a participative dialogue with various target groups. Risk communication thus goes far beyond informing all involved and interested circles, beyond assessment work in the field of antimicrobial resistance and its results. Timely information of the public regarding possible health-related risks, insights gained and working results forms the basis for this dia-

logue.

6.1.1.8.2 Scientific expert events and publications

The results of GERM-Vet monitoring and zoonosis monitoring (which includes antimicrobial resistance monitoring for certain zoonotic agents) have so far been reported to the expert community in the form of presentations and posters at corresponding expert conferences. In addition, scientific publications are written and appear in the corresponding specialist journals. The data from zoonosis monitoring are made available to the public each year in the EU Zoonosis Report and the National Zoonosis Report. The data from GERM-Vet monitoring are moreover incorporated into the GERMAP Atlas of Antimicrobial Resistance and Antibiotic Consumption, which is compiled together with contributions from experts from human medicine. Furthermore, the BVL regularly holds workshops on the methodology of MIC determination.

The aforementioned international symposia have already been held at the BfR and the BVL:

- BfR Symposium: Towards a Risk Analysis of Antibiotic Resistance, 9–11 November 2003
- BVL Symposium: Risk Management for Containing Antimicrobial Resistance, 15–16 November 2004

The “Antimicrobial Resistance” Working Group of the DVG has so far dealt with various topics, including the following activities, for example: definition of veterinary-specific, clinical limits. Veterinary-specific clinical limits are necessary for making predictions about the success of treatment when using a particular antimicrobial active substance. Accordingly, veterinary-specific clinical limits apply to one active substance, one type of animal and one particular organ system. The initial efforts of the “Antimicrobial Resistance” Working Group to define veterinary-specific limits concentrated on amoxicillin in the treatment of respiratory tract infections in pigs. Comprehensive analyses of the currently available literature on the pharmacology, pharmacokinetics and efficacy of amoxicillin in pigs permitted the provisional definition of limits for the categories “susceptible”, “intermediate” and “resistant”. The results obtained were discussed with the CLSI Subcommittee for susceptibility testing of veterinary-specific pathogens and a corresponding publication prepared, which was printed in the journal “Veterinary Microbiology” in January 2008.

6.1.1.9 Training and continuing education

The subject of antimicrobial resistance is embedded both

in training and higher education. In addition, institutions at the federal and Länder level offer detailed symposia and continuing education events to communicate new insights to the participants. In June 2008, for example, the State Health Office and the State Office for Consumer Protection and Food Safety (LAVES) of Lower Saxony cooperated to organise a symposium entitled “Zoonosis Management: A Common Task for the Public Health Service and the Veterinary Sector”, where the great importance of this topic was expressed in presentations by both agencies and subsequent discussions. The LAVES additionally holds annual events with the municipal veterinary authorities. Moreover, a continuing education event is held every two years with the departments of public prosecution of the regional courts, which are responsible for, among other things, prosecuting violations of Section 10 of the Food and Feed Code (LFGB). This event routinely includes a presentation on the subject of antimicrobial resistance, in order to also sensitise this group of persons (with respect to the importance of prosecuting MRL value transgressions for pharmacologically active substances).

Activities of the Bavarian State Office for Health and Food Safety – Academy for Health, Nutrition and Consumer Protection are a further example. On 14 June 2007, it held an interdisciplinary symposium in Munich entitled “Antimicrobial Resistance – Relevance and Prevention”, which was organised in cooperation with the following scientific societies: Paul Ehrlich Society (PEG), Antibacterial Chemotherapy Section; German Society for Veterinary Medicine (DVG), “Bacteriology and Mycology” Expert Group and “Antimicrobial Resistance” Working Group; German Society for Hygiene and Microbiology (DGHM); Permanent Working Group “Clinical Microbiology and Infectiology”; Federal Association of Doctors for Microbiology and Infection Epidemiology (BÄMI).

6.1.2 International measures

Transactions involving live animals and products of animal origin take place within the European internal market and internationally across continents. Accordingly, international measures influence the registration and use of antibiotics for veterinary medicine. The specifications for registration have been implemented nationally, and the EMEA applies harmonised Community law for central European registrations; see Chapter 6.1.1.3.

6.1.2.1 Measures at the European level

In addition to EU legislation, the European Community

addressed the problem of antimicrobial resistance in 2001 and 2008. In 2001, the Council adopted a conclusion dealing with the problem of resistance in human medicine. In 2008, numerous aspects from the veterinary sector were added, and a call on the Member States and the Commission formulated to include the veterinary sector in measures for minimising antimicrobial resistances. In addition, the European Community created possibilities for supporting research in the 6th and 7th Framework Programme. Congresses on the subject funded by the European Community are held regularly at the European level.

In the past, individual Member States established programmes aimed at minimising the antimicrobial resistances of pathogens in animals. These programmes are usually based on reducing the use of antibiotics in live animals and strict specifications for veterinary surgeons that regulate the use of antibiotics in detail.

The Committee for Veterinary Medicinal Products (CVMP) of the European Medicines Agency (EMA) has established an expert group (Scientific Advisory Group on Antimicrobials, SAGAM) that specifically addresses the subject of antimicrobial resistance in connection with central registrations. The SAGAM developed so-called reflection papers^{52–54} for reserve antibiotics that are also used in human medicine (fluoroquinolones and 3rd and 4th generation cephalosporins). They provide recommendations regarding therapeutic use and advocate more extensive notes in the draft labelling. For example, substance classes of this kind are only to be used if other antibiotics are not available or have proven to be ineffective.

In addition, the SAGAM has elaborated a reflection paper⁵⁵ that provides for a post-marketing resistance monitoring programme as a commitment in the case of centrally registered antibiotics whose resistance situation is not sufficiently clear.

6.1.2.1.1 Activities of the European Food Safety Authority

The Panel on Biological Hazards of the European Food Safety Authority (EFSA) examined the question of the extent to which, from the point of view of public health, foods serve as a source of intake by humans of antimicrobial-resistant bacteria, or of antimicrobial-resistant genes through bacteria, in order to be able to assess the ascertained risks and determine possible control measures for reducing susceptibility.

The result is that the current extent of susceptibility to antimicrobial-resistant bacteria is difficult to determine

and that the role played by foods in the transmission of resistant genes has not been sufficiently researched. According to the information available to the EFSA, bacteria transmitted through foods, including the known pathogens and commensal bacteria, are demonstrating an increasing and diverse range of resistances to key antibiotics used in human and veterinary medicine, and every further increase in the resistance of bacteria contained in foods can have an influence on human exposure.

The principles applied in avoiding and controlling the spread of pathogenic bacteria via foods also contribute to avoiding the spread of antimicrobial-resistant, pathogenic bacteria.

The development and application of new approaches is recommended for identifying and controlling foods as carriers of antimicrobial-resistant bacteria and associated genes on the basis of epidemiological studies and studies that seek to identify sources, including raw poultry, raw pork and raw beef.

The EFSA is of the opinion that special, focused measures currently ought to be defined and launched throughout Europe, in order to counteract the existing and developing resistance of known pathogenic bacteria to fluoroquinolones and (3rd and 4th generation) cephalosporins that have been found in various foods and in animals in primary production.

In summary, it is the view of the EFSA that the control of all routes via which antimicrobial-resistant bacteria and associated genes can develop in human patients – foods being just one such source – calls for a reaction on the part of all interest groups, who must face up to their responsibility for avoiding both the development and the spread of antimicrobial resistance in their respective spheres of work, which also include human medicine, veterinary medicine, primary production of food-producing animals, food processing and food preparation, as well as in the regulation of food safety.

6.1.2.1.2 Studies on antimicrobial resistance

Throughout Europe, studies of antimicrobial resistance in animals are conducted on the basis of Directive 2003/99/EC and in accordance with Regulation (EC) No. 2160/2003 as well as the ordinances issued on the basis of this Regulation. These specifications for monitoring and recording in the framework of studies are to be implemented nationally (see Chapter 6.1.1.2.2). In this context, the CRL Antimicrobial Resistance has the important task of coordinating the training of the NRLs and providing the

responsible laboratories with method recommendations.

6.1.2.1.3 Harmonisation of measures

In relation to the studies and investigations mentioned, the decisions mentioned and training by the CRL standardise the specifications for sampling and the test methods themselves. Epidemiological limits according to the recommendations of the European Committee on Antimicrobial Susceptibility Testing (EUCAST) are used as the limits for assessing the resistance of zoonotic agents at the European level. Standardisation is intended to help make the collected data comparable, thus permitting comparisons between the Member States. Beyond this, the collected data form the basis for defining prevalence targets. Consequently, Community-wide measures, harmonised to the greatest possible extent, are to ensure that the occurrence of pathogens and resistances can be minimised.

However, in addition to harmonisation of the measures for monitoring resistances, or of measures possibly resulting therefrom, the elements of antibiotic registration and pharmacovigilance in veterinary medicine are also very largely harmonised throughout Europe by the specifications of Directive 2001/82/EC. The specifications for newly registered antibiotics encompass extensive conditions regarding efficacy, the resistance situation and monitoring of resistance development, and clear regulations for use (mandatory prescription for food-producing animals). The EMEA makes a further contribution to harmonising the use of antibiotics as regards antibiotics that are centrally registered at this agency and can be used in all Member States.

6.1.2.2 Supranational measures

Animals and goods (e.g. foods of animal origin) are traded not only within the European internal market, but also between continents. Both the Food and Agriculture Organization of the United Nations (FAO), World Health Organization (WHO) and the World Organisation for Animal Health (OIE) have issued scientific statements on antimicrobial resistance and developed recommendations that should be observed in international trade. These recommendations are constantly being expanded and revised.

6.1.2.2.1 Specifications of the World Organisation for Animal Health

The World Organisation for Animal Health (OIE) has intensively studied the subject of antimicrobial resistance in relation to animal health and additionally compiled a list of antibiotics of importance in veterinary medicine. This

list served the FAO/WHO and the OIE as a basis for comparison with the use of antibiotics in human medicine, which led to the identification of antibiotics that are used in both sectors and have the potential for cross-sector antimicrobial resistance.

The Terrestrial Animal Health Code contains guidelines

- for the harmonisation of national antimicrobial resistance surveillance and monitoring programmes⁹⁸,
- for the monitoring of the quantities of antimicrobials used in animal husbandry⁹⁹, and
- for the responsible and prudent use of antimicrobial agents in veterinary medicine¹⁰⁰.

In addition, Chapter 3.9.4 of the “Terrestrial Animal Health Code” contains specifications for risk assessment for antimicrobial resistance arising from the use of antimicrobials in animals¹⁰¹.

Consequently, a national strategy relating to the health of live animals must be geared to these specifications and give consideration to these factors.

6.1.2.2.2 Specifications of the WHO/FAO (Codex Alimentarius)

The WHO and the FAO have launched a joint initiative for elaborating standards for world trade in foodstuffs with the aim of avoiding dangers for health and establishing minimum standards. The antimicrobial resistance of organisms in animals used for food production is also a topic in this context (Codex Alimentarius).

The “Code of practice to minimize and contain antimicrobial resistance” (CAC/RCP 61–2005) makes provision for a number of minimum measures to be observed on an interdisciplinary basis (registration, monitoring, training, research, etc.) in order to reduce antimicrobial resistance.

A Codex Ad Hoc Task Force of the governments on the subject of antimicrobial resistance was set up at the 29th Meeting of the Codex Alimentarius Commission (2006). Within four meetings, this Task Force has the job of elaborating scientifically sound instructions for assessment of the risk to human health arising from antimicrobial-resistant pathogens or resistance determinants in foods. The guidelines are also to encompass animal husbandry, including aquaculture. One guideline deals with recommendations for suitable risk management measures for reducing the risk to human health determined by assessment.

The existing specifications of the WHO, FAO and OIE, as well as the instruments existing at the international,

national and regional levels, are to be taken into account when elaborating guidelines on the methods and process of risk assessment. It was also found in this context that prudent use of antibiotics in animal husbandry serves animal health and that antibiotics are indispensable for treating diseased animals and animal stocks.

These specifications should be taken into account with an eye to the interdependences existing in international trading.

6.2 Future national measures for minimising antimicrobial resistances

The risk of transmission of antimicrobial resistances or resistance determinants is to be assessed on a scientifically sound basis, and there is to be further, detailed research into the background, processes and developments that lead to resistant organisms in animals, or to transmission between animals and humans. New measures for minimising the occurrence of resistances must be taken on this scientific basis. They must give consideration to safeguarding consumer health protection (human health), minimising infectious diseases in animals, and the necessity of effective antibiotics in animal healthcare to restore the health of animals. They must likewise be suitable for safeguarding international trade.

To do justice to these requirements, measures are also to be taken in the spirit of the principle of prevention if there is sufficient information indicating a need for action. In this case, too, the measures taken must stand up to scientific verification, or be adapted accordingly.

The actual situation described above, as regards measures for minimising antimicrobial resistances in the field of animal husbandry, the food chain and veterinary activity, directly gives rise to a need for additional measures, described in more detail below. Furthermore, Chapter 6.3 presents the research and development work required to achieve the fundamental targets as described in Chapter 4.2.2.

6.2.1 Recording of the quantities of antibiotics sold

Recording of the quantities of substances with antimicrobial action sold is a fundamental criterion for assessing the antimicrobial resistance situation in veterinary medicine. To this end, there is a need to record the quantities sold (i.e. the quantities sold to veterinary surgeons by pharma-

ceutical manufacturers) on a regional basis and in such detail that a regional link can be established between these quantities for the respective antibiotic in question and regional resistance data to assess the resistance risk. For this reason, the legal possibilities for recording the quantities of antibiotics sold according to Section 47 Para. 1c AMG are currently being worded in such a way that detailed recording of the quantities sold is possible. The concrete details are then to be formulated in the framework of an ordinance.

6.2.2 Recording of the quantities of antibiotics used

The information obtained in the research project – mentioned in Chapter 6.1.1.4.2 – on the representative recording of the quantities of antibiotics used is in future to be reviewed and, if appropriate, used for regulations in drug law on the obligatory recording of the quantities of antibiotics used in food-producing animals. The data then to be expected from the recording of quantities used are to be consulted by the higher federal authorities for ongoing assessment of the risk of antimicrobial resistance development.

6.2.3 Expansion of resistance monitoring

Any expansion of resistance monitoring is to build on the scientifically sound basis of the resistance situation data already available and yet to be obtained. A distinction must be made between monitoring aimed at animal health and monitoring aimed at consumer health protection (human health).

Based on the latest findings, a plan for monitoring antimicrobial resistance in the food chain is elaborated annually and thus adapted to current developments. Building on extensive collections of strains at the NRL Antimicrobial Resistance, originating from samples submitted by the Länder, not only is more extensive characterisation performed, but new developments are also assessed retrospectively. Representativeness in terms of different microorganisms and influencing factors (e.g. housing forms for animal species, region, accompanying clinical and therapeutic circumstances) is increasingly being improved in this context. Direct and indirect transmission mechanisms via different exposure routes are taken into account in the interdisciplinary assessment of resistance development.

The data from the studies to date (GERM-Vet and GERM-Vet-BfT) are to be taken into account for monitoring

antimicrobial resistance in animals with a view to animal health, and the measures taken are to be expanded on this basis following scientific verification. Following assessment of the isolates collected, the monitoring of zoonotic bacteria is also to be established for non-food-producing animals.

The data from both areas are then to be used for comprehensive risk assessment, which will subsequently lead to scientifically based risk management measures in a wide variety of fields, including registration.

6.2.4 Standardisation of resistance determination

The standardisation of resistance determination is closely linked to the monitoring activities and the targeted use of antibiotics for therapeutic purposes. To be able to use data from extensive monitoring for comprehensive risk assessment and to derive binding measures, the data must be comparable. Consequently, standards must be created for sampling, cultivation of the organisms and methodical determination of the resistance characteristics and evaluation. Susceptibility tests must adhere to internationally acknowledged method specifications. In this context, EFSA recommendations already exist, as do standards binding throughout the EU, for the field of zoonotic agents and commensal organisms (microorganisms that are neither harmful nor useful). The EUCAST has already elaborated epidemiological limits (cut-off values) for this purpose, which permit early detection of incipient resistance development. These cut-off values can be used to examine and assess monitoring data from the human and veterinary sectors. Whether and to what extent further epidemiological limits are to be developed in individual instances, or arise retrospectively from the examination and assessment of the monitoring data, is to be investigated in collaboration with the EUCAST.

In the framework of therapeutic use of antibiotics, the “Antimicrobial Resistance” Working Group of the DVG recommends adherence to the specifications of CLSI Document M31-A326 for routine veterinary medical diagnosis. However, standards of this kind should also be given a minimum of definiteness by legislation. This could be realised through European coordination. To start this process, further clinical limits are, for example, to be developed for the MIC values for specific antibiotics – especially also for antibiotics that have been registered for a long time.

All stakeholders must be involved when defining limits. To what extent epidemiological or clinical limits need to be

consulted for assessing resistance will depend on the intended use. On the one hand, the clinical limit plays a decisive role in interpreting the results of in vitro susceptibility testing for the treatment of sick animals. It gives the treating veterinary surgeon an indication of the antibacterially active substance that is most probably therapeutically effective against the disease in question. On the other hand, epidemiological limits distinguish a presumably susceptible subpopulation (wild-type population) from a presumably resistant subpopulation. Based on this distribution, a switch of a susceptible population to a population with reduced susceptibility can be assessed, and incipient resistance development thus detected. This makes it possible to assess the threat to humans in relation to the aspect of public health.

6.2.5 Monitoring of antibiotic efficacy

According to Section 63b AMG, the pharmaceutical manufacturer is required to submit regularly updated reports on the safety of the medicinal products it puts into circulation (Periodic Safety Update Report, PSUR). These reports are to be examined by the BVL. The drug risks to be taken into account in this context include the development of antimicrobial resistance (General Administrative Regulation on the Graduated Plan). The data presented in PSURs primarily consist of spontaneous reports of clinical observations. Resistance data from curative practice are only rarely communicated via the spontaneous reporting system and do not permit assessment of the general resistance situation. Independently of these individual assessments, it is therefore necessary to perform ongoing, representative resistance monitoring in relation to the efficacy of all antibiotics used in veterinary medicine. This monitoring, which is already performed to a limited extent by the BVL (see Chapter 6.2.3, third paragraph) is to be implemented legally, in which context it should be possible to give priority to certain substance groups. Pinpoint resistance monitoring is particularly to be performed for the antibiotics classified as critical in veterinary medicine. As recommended by the EMEA, these include 3rd and 4th generation cephalosporins and fluoroquinolones, for example. The information gained from these measures is to be used for risk assessment and risk management. In the case of new registrations, the results of existing monitoring programmes are already incorporated in the form of special notes in the draft labelling, or entail appropriate requirements if the resistance situation is unclear. A further objective is to use data obtained from monitoring for the post-marketing sector as well in the framework of prolongation and pharmacovigilance. If necessary, they are likewise to be incorporated in the draft labelling or

entail appropriate, more extensive measures in the event of increased resistance development.

6.2.6 Annual antimicrobial resistance report

At the moment, the resistance results of GERM-Vet (zoonotic agents) are published in the scientific press, while those on zoonotic agents (Salmonella, Campylobacter, E. coli, MRSA) are published in the framework of the National Zoonosis Trend Report and thus in the European Zoonosis Trend Report. Results from pharmacovigilance generally lead to measures relating to the registration of a specific product, but are not automatically included in the risk assessment of the overall situation and the publication.

The question is being examined of whether the data obtained at these different levels, and their assessment, can be made accessible to the general public in summary form. Beyond this, it is important that all data are included in the assessment of the antimicrobial resistance situation in veterinary medicine. Risk management must then be performed on the basis of scientific criteria and in compliance with international specifications, the interests of consumer health protection and the requirements of animal health. The report should summarise all these aspects. The interface between humans and animals should be given particular consideration in this context.

6.2.7 Antibiotic guidelines

The antibiotic guidelines are to be updated and regularly adapted to the state of the art in veterinary medical science. The BMELV is examining whether these guidelines should be given a more binding nature in order to achieve the objectives of the strategy (Section 56a Para. 5 AMG). It must be borne in mind that acceptance of the guidelines by the veterinary community must be ensured.

6.3 Research into antimicrobial resistance and the avoidance of

antimicrobial resistance

6.3.1 Antimicrobial resistance research activities in the portfolio of the BMELV

Various institutions in the portfolio of the BMELV have been addressing issues relating to exploring antimicrobial resistance phenomena for a long time, in some cases for more than 20 years and at an internationally acknowledged level. These institutions include:

- The Federal Institute for Risk Assessment (BfR),
- The Federal Office for Consumer Protection and Food Safety (BVL), and
- The Friedrich Loeffler Institute (FLI).

The BfR handles research projects on improving diagnostic methods and on antimicrobial resistance in connection with bacteria that are of importance for human health in order to optimise routine diagnosis. Molecular biological characteristics of pathogens in relation to antimicrobial resistance are primarily explored in food-relevant bacteria (*Salmonella*, *Campylobacter*, *E. coli*, MRSA, *Yersinia*). They are studied in terms of their resistance genes and other structures of importance for the transmission of resistances from animals to humans. One focus is projects concerning resistance to fluoroquinolones and cephalosporins, the antibiotic groups acknowledged by the WHO/FAO/OIE as being particularly relevant to human medicine. A project on recording the quantities of antibiotics used is also in progress (see Chapters 6.1.1.4.2 and 6.2.2). Apart from this, the BfR plays a key role in the monitoring tasks relating to antimicrobial resistance in pathogens of significance for human health. This monitoring covers the national data on antimicrobial resistances from the food chain and from specific fundamental pan-European studies. The BfR operates the NRL Antimicrobial Resistances for the food chain.

On special issues for clarifying the MRSA situation in Germany, the BfR manages and coordinates studies for recording the occurrence of MRSA (including Länder participation). Epidemiological and diagnostic questions are also to be answered, and risk assessments performed. Some of these questions are also part of studies conducted by third parties.

The BVL performs studies on antimicrobial resistance trends in zoonotic agents in live animals (food-producing animals and “hobby” animals). The findings are used for assessing the registration of antibiotics.

The FLI deals with issues relating to resistance genes and resistance mechanisms, generally at the molecular level, and draws up recommendations for daily clinical practice. Examples include the following:

- Elaboration of the methodology for determining the susceptibility of bacterial pathogens of relevance in veterinary medicine on the basis of specific examples (*Haemophilus parasuis* (pigs), *Riemerella anatipestifer* (poultry), *Rhodococcus equi* (horses)),
- Examination of the molecular foundations of antimicrobial resistance (resistance genes, resistance mechanisms and resistance mutations) in economically significant zoonotic agents (e.g. *Pasteurella*, *Manheimia*, *Haemophilus*, *Actinobacillus*, *Rhodococcus*, *Riemerella*, *Bordetella*),
- Performance of preliminary research into resistance to new, relatively new or future veterinary antibiotics (externally funded research),
- Performance of selected pathogen/active-substance resistance projects of major economic, scientific and medical (both human and veterinary medical) importance for
 - Penicillin resistance in *Streptococcus suis*,
 - Extended-spectrum β -lactamases (ESBL),
 - Transmissible quinolone resistance,
 - Antimicrobial therapy options for MRSA (oxazolidinone, glycopeptide, pleuromutilin resistances),
- Characterisation of mobile genetic elements in the transfer of resistance characteristics (host cell spectrum, co-localisation of resistance, co-selection potential).

The FLI will additionally clarify certain questions relating to the molecular characteristics of MRSA. This is intended to provide information on the risk potential and the potential capabilities of the commensal organisms of the mucosa.

6.3.2 Research and development requirement

The previous measures described indicate a substantial research and development requirement that can essentially be divided into two areas. First, there is a need to clarify questions relating to the origin, spread and transmission of resistances and resistance genes, including the diagnostic methods for determining an existing infection. To create alternatives to the use of antibiotics in animals, there is also a substantial need for research into, and promotion of, the development of vaccines and similar products that enable animal immune systems to control infec-

tions without the use of antibiotics, or to create conditions that prevent infections from the outset (hygiene).

6.3.2.1 Antimicrobial resistance characteristics and mechanisms

So that assessment of the risk of transmission of antimicrobial resistances or resistance determinants can be put on a sound, scientific footing, and the background, processes and developments leading to resistant organisms in animals, or to transmission between animals and humans, can be explored, the BMELV is of the opinion that there is a need for research in the framework of consumer health protection. The resistance genes and mechanisms of many pathogens of relevance in veterinary medicine are unknown. Clarifying these aspects can be seen as part of the preliminary research into resistances to new, future veterinary antibiotics. Although knowledge exists regarding a number of resistance development mechanisms and the fact that animals and products of animal origin are contaminated with resistant organisms or resistance determinants, there is an urgent need to clarify how resistant pathogens – e.g. multiresistant *Escherichia coli* (*E. coli*) – get into certain habitats in the animal organism, or how and why they develop there (e.g. in the intestinal tract of cattle). In only few instances do we know how these pathogens acquire diverse resistance mechanisms, pass them on, and whether they then also reach humans, be it by direct transmission of the pathogens or by food-induced transmission. Another of the questions additionally to be clarified is whether the potential properties are actually used and whether further properties – e.g. virulence properties – can possibly be acquired, above and beyond the resistance characteristics.

When applying the measures for minimising antimicrobial resistance in the field, there is the problem that every resistance test to date is dependent on isolation of the organisms. In acute cases, antibiotics can only be given to an animal following clinical diagnosis. Before administering the first dose, a sample can be taken to isolate and cultivate the organism, so that the resistance characteristics can subsequently be determined. However, the results are usually only available several days later, meaning that the veterinary surgeon initially has to select and use an antibiotic on the basis of his knowledge and experience with the clinical picture, although the resistance of the causal organism or other commensal organisms has not yet been determined. This makes it difficult not only to carefully select an antibiotic, but also to apply the above-mentioned guidelines of the German Veterinary Association in practice. In this context, it must be examined whether rapid tests can be developed that permit estima-

tion of the resistance situation, both on-site and when selecting an antibiotic and further therapeutic steps.

The BMELV is of the opinion that collaboration with the human medicine sector is necessary in these fields.

6.3.2.2 Promotion of the development of alternatives to the use of antibiotics

In veterinary medicine, antibiotics are approved as veterinary medicinal products for therapy or for metaphylaxis^{f)}. Group and herd treatment of infectious diseases is often unavoidable in agricultural livestock. However, in addition to the occurrence of the pathogens, there are other factors of decisive importance in this context. Infectious diseases are also a management problem where, on the one hand, husbandry or hygiene measures are not performed effectively and, on the other hand, possibilities for prophylactic treatment by vaccination are either not consistently utilised or do not exist. If no vaccines are available, the development of new vaccines can help to remedy the situation.

One sustainable example is the use of vaccines in aquaculture in Norway. In this case, introduction of the vaccination of salmon against vibriosis and furunculosis led to a decline of more than 80 % in the use of antibiotics, while the population doubled (see Fig. 3).

Transferring an effect of this kind to other fields of animal husbandry is to be the objective of promoting vaccine

f) Exception: prophylaxis for drying off dairy cows or in the perioperative field, for example.

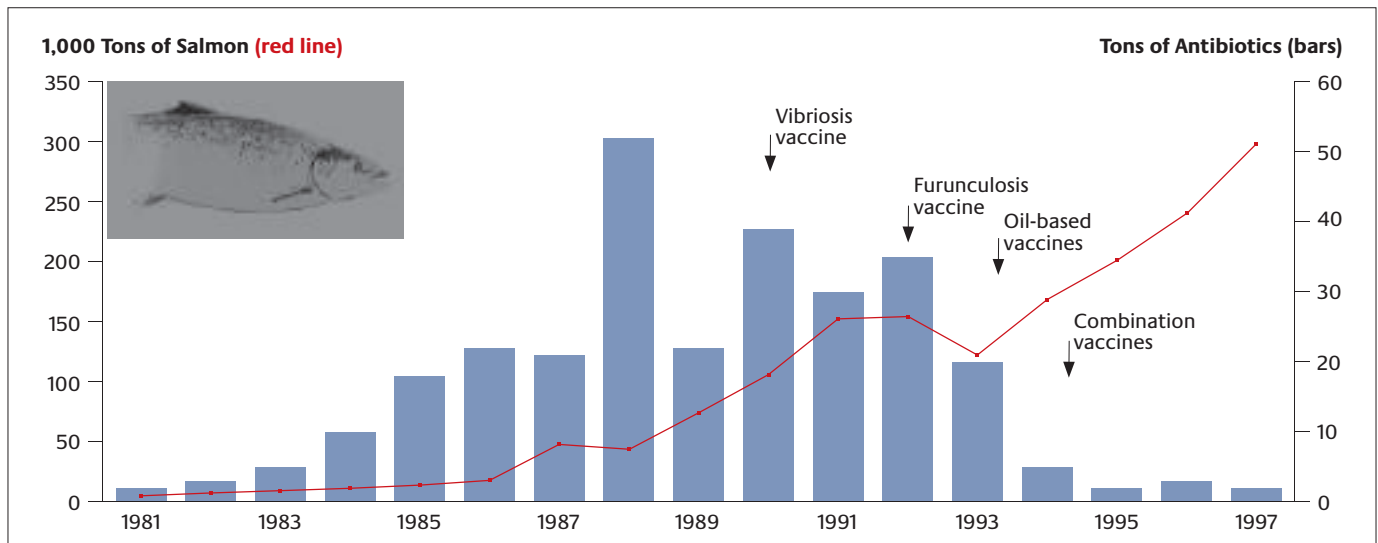


Fig 3. Impact of the use of vaccines on antibiotic consumption, after Varma 2008; IFAH Europe Annual Conference, Brussels, 12 June 2008: “Animal health solutions for the future”

development. Not only vaccines aimed directly at bacteria have the effect of reducing the quantities of antibiotics used, but also vaccines that prevent infections (e.g. viral infections, infestation with parasites, etc.) potentially leading to bacterial secondary infections. Developments must aim to enable the establishment of vaccines in the everyday practice of routine animal husbandry. Product developments of this kind contribute directly to consumer health protection.

In addition to promoting vaccines, the question must also be examined of the extent to which other alternatives, such as immunomodulators or so-called competitive exclusion preparations or other substances that strengthen the immune system, can contribute to reducing the quantities of antibiotics used in animal husbandry.

Management in animal husbandry influences the health of the animals and the quantities of antibiotics used, and is thus a significant focus for research. The question must be examined as to whether and to what extent the occurrence of infectious diseases resulting in use of antibiotics can be reduced by optimising management measures in animal husbandry (e.g. hygiene, feeding, animal transport).

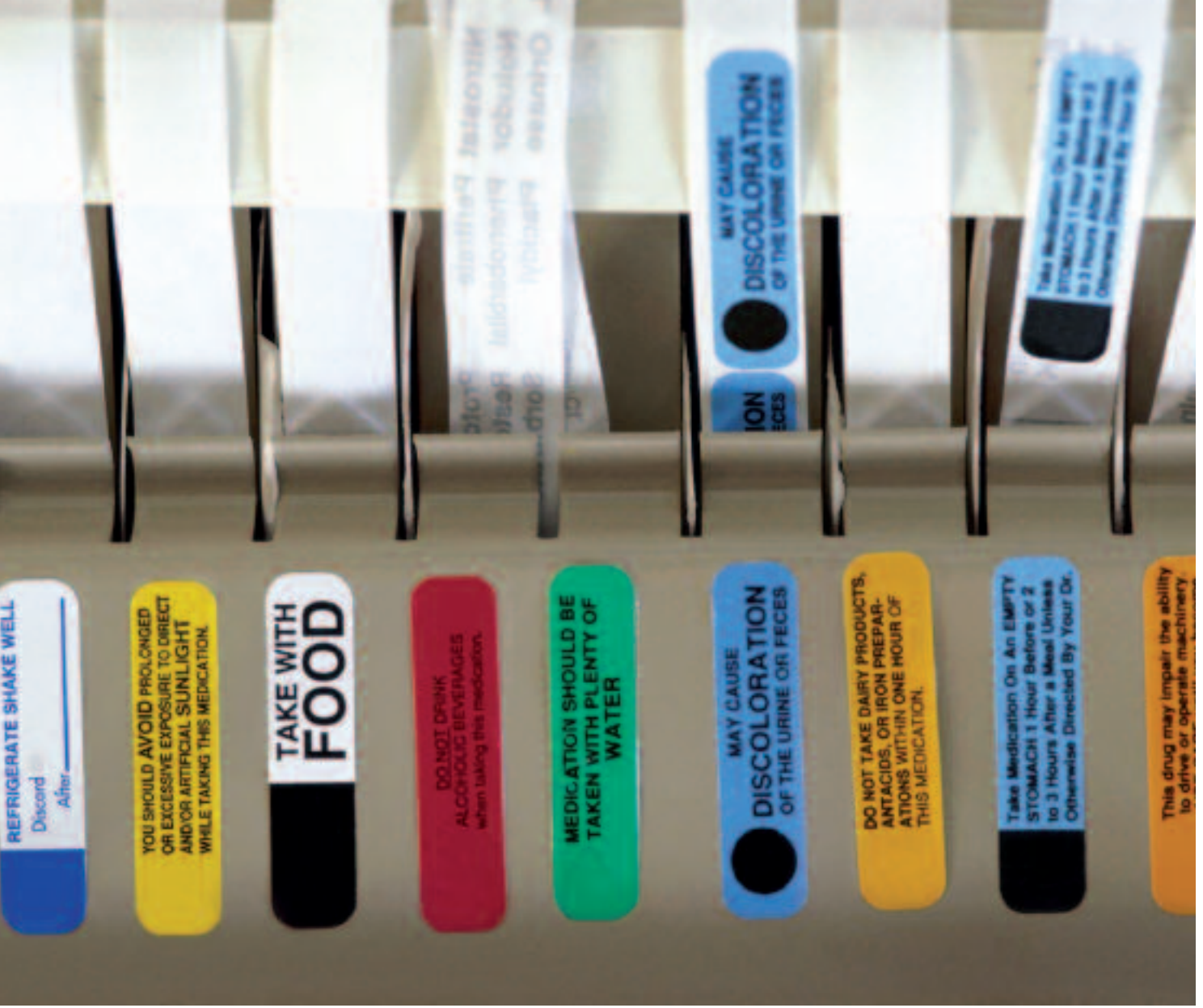
The BMELV sees an urgent need for research and development activities in connection with these alternatives.

6.3.2.3 Promotion of research into the optimisation of antibiotic and vaccine use, and into the

optimisation of monitoring

To achieve optimum results when using antibiotics themselves, or existing alternatives, it may be necessary to promote research geared to their optimisation, so that there is the possibility of using available means to reduce the use of antibiotics, and thus the selection pressure on existing bacteria.

Monitoring measures should be optimised in such a way that the spread of a resistance can be detected at an early stage and the data support modelling of future spread. Of decisive importance in this respect is the interdisciplinary networking of knowledge at all levels of the food chain and in humans. In particular, the objective must be to identify factors that favour a spread and to estimate the efficacy of countermeasures in advance.



Appendix, References

1.1 Overview of the planned structure

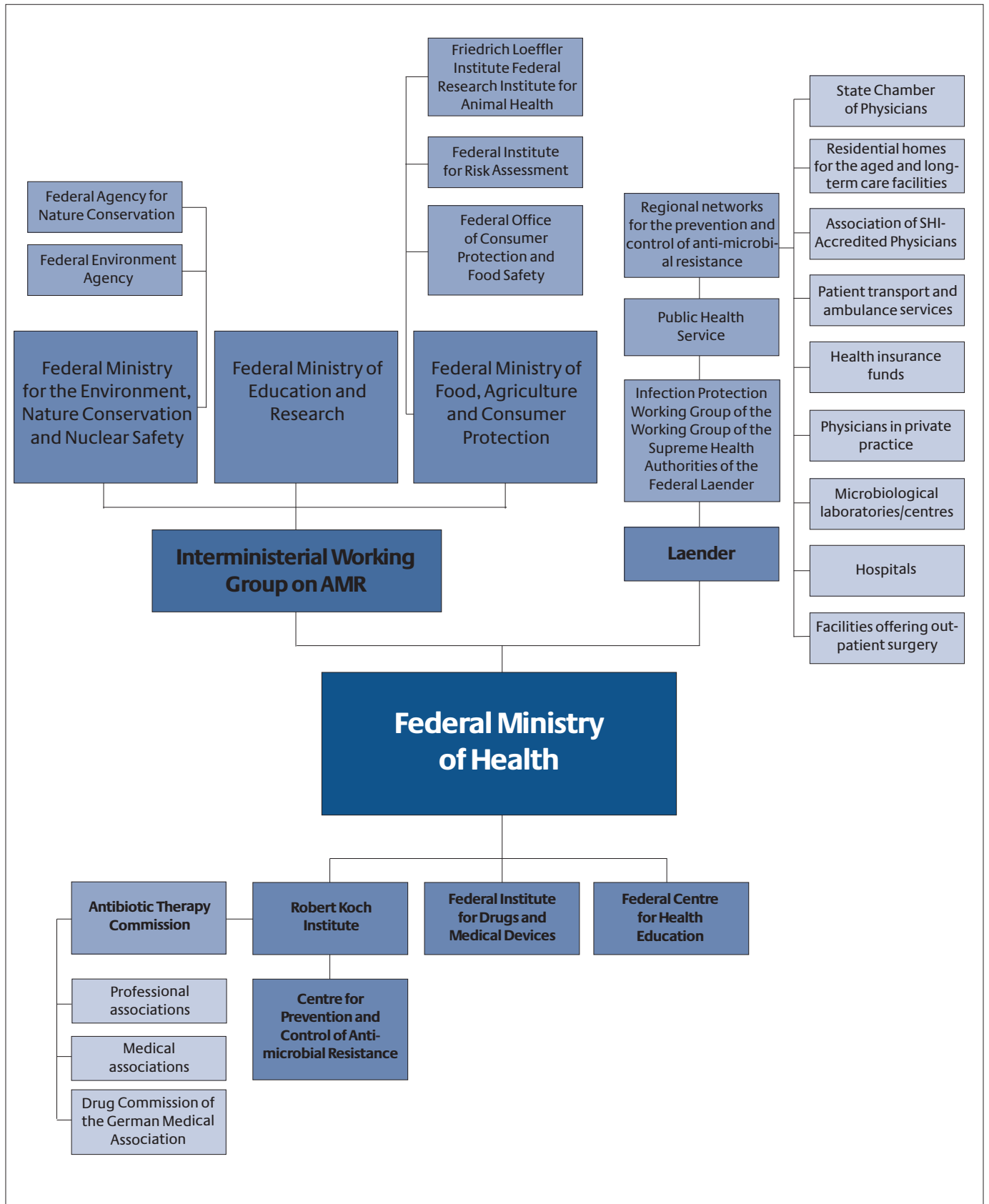


Fig 4. Overview of the planned structure

1.2 Overview of the actions planned in the field of human medicine

Goal	Actions	Milestones
1.1	Compilation of acknowledged recommendations for the recording and analysis of data on antimicrobial resistance	by the end of 2009
	Integration of existing surveillance projects with a general survey approach and based on existing structures, as well as establishment of a central database; recruitment of new participants. long-term support and maintenance of the database on surveillance of antimicrobial resistances	starting in 2008
	Review of data on antimicrobial resistance from existing surveillance projects with a specific survey approach as regards quality and comparability, and pooling of the data from these projects in annual reports	by the end of 2009
	Joint use of the antimicrobial resistance database by the Robert Koch Institute and the Federal Institute for Drugs and Medical Devices	starting in 2010
	Expansion of compulsory notification according to Section 7 Para.1, first sentence, IfSG to include the detection of MRSA in blood or liquor and the detection of toxin A or B of Clostridium difficile in faeces	by mid-2009
1.2	Compilation of acknowledged recommendations for the recording and analysis of data on antibiotic consumption	by the end of 2010
	Review of data on antibiotic consumption from other monitoring projects (e.g. SARI and MABUSE) as regards quality and comparability, and pooling of the data from these projects in annual reports	by the end of 2010
	Recruitment of new participants, and long-term support and maintenance of the database on monitoring of antibiotic consumption	starting in 2009
	Introduction of voluntary antibiotic consumption monitoring in hospitals	by the end of 2009
2.1	Survey of the participants in the antimicrobial resistance surveillance system and establishment of a feedback system	by the end of 2009
2.2	Identification of the work capacity for advanced diagnostics/studies of (multi)resistant pathogens for which no National Reference Centre currently exists	by the end of 2009
	Identification and appointment of an institution catering to the requirements for advanced diagnostics/studies of (multi)resistant pathogens	by the end of 2009
2.3	Establishment of an early-warning system	by the end of 2010
2.4	Development of indicators for antibiotic use and antimicrobial resistance	starting in 2009
	Examination of integration of the indicators in the external quality assurance of the institution according to Section 137a and in the Quality Report according to Section 137, Para. 3, first sentence, No. 4	starting in 2009
	Introduction and application of quality indicators, e.g. in the framework of the AQIUK project (Outpatient Quality Indicators and Indices) of the KBV	starting in 2009
3.1	Establishment of an Antibiotic Therapy Commission at the Robert Koch Institute	by mid-2009
	Preparation of general principles for antibiotic therapy, compilation of nationally acknowledged recommendations and guidelines, initiation of the preparation of necessary guidelines	starting in 2010
	Evaluation of the application of recommendations for antibiotic therapy	starting in 2013
3.2	Examination of the possibilities for improving cooperation between responsible organisational units in hospitals	starting in 2009

continue on page 58

Goal	Actions	Milestones
4.	Review of the eligibility for reimbursement of diagnostic procedures and possible obstacles to their application, as well as identification of deficits and problems in connection with quality assurance in diagnosis	starting in 2009
	Review of the importance of, and preparation of, recommendations for the use of (rapid-test) diagnosis in private practices and hospitals	2009 and 2010
5.	Elaboration of proposals for increasing emphasis on the topics of antimicrobial resistance and patient communication in the basic training, specialist training and continuing education of physicians, pharmacists and nursing staff	by mid-2009
	Review of the possibilities for more firmly establishing the subject of antimicrobial resistance in natural science study courses, especially in the study of biology	by the end of 2009
	Establishment of a certified continuing education programme for qualification as NIP/ABS Officer (NIP = Nosocomial Infection Prevention, ABS = Antibiotic Stewardship)	starting in 2009
6.1	Pilot projects for creating regional networks for prevention and control of antimicrobial resistances in selected areas	by the end of 2009
	Evaluation of the regional networks and adaptation of the intervention measures following evaluation by the Laender/Public Health Service	starting in 2012
	Implementation of workshops for network moderators in the Public Health Service	2009
6.2	Establishment of an Interministerial Working Group on Antimicrobial Resistance for interdisciplinary coordination, planning, evaluation, adaptation and expansion of national antimicrobial resistance policy	by mid-2008
6.3	Establishment of an agency at the RKI for assessment and advice on the field of antimicrobial resistance, e.g. a "Centre for Prevention and Control of Antimicrobial Resistance"	by the end of 2008
7.	Strengthening of German participation in international projects and networks, e.g. EARSS and ESAC	by the end of 2010
8.	Study of the antibiotic prescribing practices of physicians in Germany (funding has already started)	by the end of 2008
	Survey of patients on the correct intake of antibiotics and their expectations of physicians when it comes to prescribing antibiotics	by the end of 2009
	Evaluation of the German National Strategy on the Diagnosis, Prevention and Control of Antimicrobial Resistance	continuously
	Adaptation of the Strategy on the Diagnosis, Prevention and Control of Antimicrobial Resistance	continuously
9.	Examination of the need for, and feasibility of, an Internet-based platform on antimicrobial resistance	by the end of 2009
	Development of an information sheet on the safe use of antibiotics, and expansion of the information on common illnesses in the cold months for which antibiotics are used, in the framework of the Health Information for the Public	by the end of 2008
	Recommendation on use of the Health Information for the Public of the IQWiG by health insurance funds to educate and inform insureds	starting in 2009
	Provision of specific information offerings for SHI-accredited physicians, e.g. in the context of quality circle work	starting in 2009
	Target group-oriented selection, preparation and forwarding of information in the field of antimicrobial resistance	starting in 2009
	Review of the possibility of, and need for, further education and information for the public	starting in 2009
10.	Determination of deficits and problems in research in the field of antimicrobial resistance in Germany	by the end of 2009

Fig 5. Overview of the actions planned in the field of human medicine

Implementation/realization of the strategy in the field of human medicine

Goal	01/2008	02/2008	01/2009	02/2009	01/2010	02/2010	01/2011	02/2011	01/2012	02/2012	01/2013	02/2013
1.1												
1.2												
2.1												
2.2												
2.3												
2.4												
3.1												
3.2												
4												
5												
6.1												
6.2												
6.3												
7												
8												
9												
10												

Fig 6. Implementation/realization of the strategy in the field of human medicine

The German Antimicrobial Resistance Strategy is to be implemented by all players in a step-by-step process. For this purpose, actions have been defined and tasks assigned to the responsible participants. The first actions are to be implemented as early as 2008. Implementation of the strategy, meaning the associated objectives and actions, is to be described during the implementation process and subjected to ongoing evaluation by the ECDC.

1.3 Projects and activities in Germany in the field of antimicrobial resistance in human medicine

The section below describes individual projects and activities for collecting and evaluating data on antimicrobial resistance and antibiotic consumption, as well as preventing and controlling antimicrobial resistance in human medicine.

1.3.1 Surveillance of antimicrobial resistance

The surveillance of antimicrobial resistance is necessary to detect changes in resistance development. Existing activities in Germany are presented below, including their objectives, special features and limitations, as well as current data.

Documentation, evaluation and retention requirements according to Section 23 Para. 1 IfSG^{79,72,102}

Responsible:

Legal basis: BMG; implementation: heads of hospitals and facilities offering outpatient surgery

Objectives:

To collect and evaluate data on pathogens showing specific resistance characteristics as a starting point for surveillance-based self-control, and for avoiding the spread of pathogens that are difficult to treat in medical care facilities; early-warning system

Special features:

Target pathogens defined by the Robert Koch Institute; continuous collection of data on pathogens showing specific resistance characteristics; data retention period of ten years; responsible public health office has access to records; failure to comply with regulations is fined as per Section 73 Para. 1 Nos. 9 and 10 IfSG

Limitations:

Data are in some cases not put to sufficient use for the purpose of self-control; medical facilities are not subject to

mandatory notification, but only mandatory documentation of pathogens showing specific resistance characteristics; no regional or supraregional pooling of data; question of quality control remains open

German Network for Antimicrobial Resistance Surveillance (GENARS)^{6,74}

Responsible:

Robert Koch Institute

Objectives:

Early-warning system for prompt recording of the current resistance situation and its development in maximum-care hospitals in Germany

Special features:

Recording of all clinical isolates from routine diagnosis; use of comprehensive, uniform diagnostic procedures, including quality control, online data transmission

Limitations:

Non-representative network of 6 microbiological university laboratories; no feedback system to prescribing physicians

European Antimicrobial Resistance Surveillance System (EARSS)^{33,38}

Responsible:

Robert Koch Institute

Objectives:

To establish a European network of national systems for the surveillance of antimicrobial resistance in order to collect and evaluate antimicrobial resistance data

Special features:

Comparative European data from 31 countries with a total of 764 microbiological laboratories and 1,185 hospitals (2006) for the purpose of analysing trends in the development of resistance among pathogens that cause invasive infections; external quality control

Limitations:

Seven selected infective agents from special clinical materials; participating laboratories/hospitals represent only 2 % of the German population and focus on the inpatient sector; no online data transmission; funding by the EU Commission is expiring

Antimicrobial Resistance Surveillance in Germany (ARS)⁹⁶

Responsible:

Robert Koch Institute

Objectives:

To establish a basis for recording the epidemiological situation of antimicrobial resistance in Germany

Special features:

Establishment of, above all, technical prerequisites for nationwide recording of the resistance situation in Germany; enables future analysis by type of care, region, time and influencing factors; establishment of a representative network for recording and evaluating antimicrobial resistance data for Germany; network structure could be used to collect antibiotic consumption data

Limitations:

Limited financing, as the project is a departmental research project of the BMG

National Reference Centres and consultant laboratories for various pathogens¹⁰⁹

Responsible:

Various (university) institutes, funding by the BMG

Objectives:

Epidemiological analysis and assessment of resistance development; improvement and standardisation of diagnostic methods, and participation in the elaboration of recommendations (e.g. diagnostics and treatment) for selected infective agents

Special features:

High standards in molecular epidemiology (in the field of pathogen typing, resistance gene detection, etc.); conclusions about the mechanisms of resistance development; in some cases, establishment of networks and studies to improve representativeness (e.g. ResiNet and KISS, see also further below)

Limitations:

Data are not representative; analysis of preselected strain material; data do not support a general trend analysis; selection of pathogens is limited to existing National Reference Centres; data available only locally at the National Reference Centre

ResiNet^{78,107}

Responsible:

National Reference Centre for Helicobacter Pylori at the Institute for Medical Microbiology and Hygiene, University Medical Centre Freiburg

Objective:

To analyse and assess resistance development in Helicobacter pylori for the purpose of elaborating treatment recommendations in a multicentre sentinel study

Special features:

Fifteen microbiology centres throughout Germany; uniform application of standardised diagnostics at all test centres; development of national H. pylori guidelines for diagnosis and therapy based on resistance data

Limitations:

Limited to Helicobacter pylori; majority of study centres located in western Germany

Hospital Infection Surveillance System (KISS)^{61-64,85,106}

Responsible:

National Reference Centre for the Surveillance of Nosocomial Infections at the Institute for Hygiene and Environmental Medicine, Charité – Universitätsmedizin Berlin

Objective:

To establish a uniform method for the surveillance of infections contracted in hospital (nosocomial infections)

Special features:

A total of 9 modules concentrating on special risk areas within a hospital; focus on certain patients (e.g. NEO-KISS), specific wards (e.g. ITS-KISS) or pathogens (e.g. MRSA-KISS); participants enter data online; central analysis of resistance data; feedback of resistance and infection rates to participants

Limitations:

ITS-KISS tracks a total of 4 resistant infective agents in intensive care; question of quality control remains open

Resistance Study of the PEG^{82,83}

Responsible:

Paul Ehrlich Society for Chemotherapy (PEG)

Objective:

To study the extent and tendencies of resistance development in clinically important species of bacteria in Central Europe

Special features:

Data have been collected every three years since 1975; data from 20 to 30 similar study centres in Germany, Switzerland and Austria; central and uniform application

of standardised diagnostics

Limitations:

Data are not collected continuously; most study centres are in maximum-care hospitals

Competence Network for Community Acquired Pneumonia (CAPNETZ)⁸⁰

Responsible:

Ulm University Hospital, Department of Medical Microbiology and Hygiene (financed by the BMBF)

Objective:

To collect reliable data on the range of pathogens, on the resistance of the pathogens to antibiotics and on the course of community acquired pneumonia in Germany

Special features:

Antimicrobial resistance data from the outpatient sector; 15 study centres across Germany; uniform application of standardised diagnostics at the test centres; by networking various national groups from all fields of medicine, new data specific to Germany can be collected; cooperation between physicians in private practice, hospital physicians, microbiologists, virologists, epidemiologists and computer scientists; about three percent of all patients (approx. 6,000) with community acquired pneumonia are to be included in the study nationwide; all clinical and microbiological data are to be pooled and a central material and data base is to be established; plans to make results available via the Internet on a multidimensional information and discussion platform for physicians and patients; CAPNETZ foundation established in autumn 2007 to optimally exploit the results and ensure continuation even after federal funding expires; the BMBF invested approx. € 14.5 million in the project

Limitations:

Data only available locally; network limited to one disease

Central Office for the Evaluation of Resistance Data on Systemic Antibiotics (Z.A.R.S.)^{18,120}

Responsible:

- Initiating and controlling institution: Federal Institute for Drugs and Medical Devices (BfArM)
- Participating institutions: Pharmaceutical industry associations, German Society for Hygiene and Microbiology, Paul Ehrlich Society for Chemotherapy (PEG), Robert Koch Institute and representatives of the Competence Network for Community Acquired Pneumonia (CAPNETZ)

Objective:

To establish a database with antimicrobial resistance data for marketing authorisation decisions based on a European Directive (CPMP/EWP/558/95 rev 1)

Special features:

Extensive database containing published data on antimicrobial resistance in Germany, particularly from the projects outlined above

Limitations:

Creation of the database is financed by the pharmaceutical industry; data are not representative, particularly for the outpatient sector

Antimicrobial Resistance Monitoring in Lower Saxony (ARMIN)

Responsible:

Lower Saxony State Public Health Office

Objective:

To collect and observe the development of resistance in clinically relevant bacteria in the inpatient and outpatient sectors

Special features:

Outpatient sector included since 2007; data are made available to the professional public; online transmission possible

Limitations:

Limited to 5 laboratories in Lower Saxony

1.3.2 Antibiotic consumption

The surveillance of consumption is necessary to identify changes in the use of antibiotics. Antibiotic consumption in Germany already is being tracked in several projects. The most important projects are presented below, indicating their objectives, special features and limitations, as well as current data:

Scientific Institute of the Local Health Care Funds (WIdO)/University Medical Centre Freiburg^{70,112,113}

Responsible:

WIdO/University Medical Centre Freiburg

Objective:

To analyse antibiotic consumption in the outpatient sector based on prescriptions charged to the statutory health insurance funds (GKV)

Special features:

Data can be analysed by substance class, physician's speciality field or individual physicians, age group and region; the diagnoses that led to treatment can be analysed; data

assessed regularly (Drug Prescription Report, GKV Rapid Drug Information); data available to physicians on a federal and regional level, and individually

Current data:

Increase in the prescribing of reserve antibiotics in the outpatient sector, although antibiotic consumption was steady after 1991 and has been declining slightly since 2001; antibiotic consumption in western Germany (Rhineland-Palatinate) is up to 50 % higher than in eastern Germany (Brandenburg); over 50 % of antibiotics are prescribed by general practitioners

Surveillance of Antibiotic Use and Bacterial Resistance in German Intensive Care Units (SARI)^{88-91,105,119}

Responsible:

Institute of Environmental Medicine and Hospital Hygiene (Department of Environmental Health Services), University Medical Centre Freiburg

Objective:

To establish a surveillance and reference data system for antibiotic use and antimicrobial resistance in intensive care units among KISS participants

Special features:

Resistance can be assessed in relation to antibiotic consumption; semi-annual feedback to participants; surveillance of 13 infective agents in intensive care units

Limitations:

A total of 45 intensive care units; calculation of antibiotic consumption is very complex; no online data transmission; lack of funding (formerly funded by the BMBF)

Current data:

Antibiotic consumption and resistance rates have generally increased in intensive care units; participation in SARI leads to a reduction in antibiotic consumption and antimicrobial resistances

Medical Antibiotic Use Surveillance and Evaluation (MABUSE Network)^{19,35,36,77}

Responsible:

Clinical research group at the Centre for Infectious Diseases, University Medical Centre, Freiburg (financed by the BMBF)

Objective:

To create a hub for clinical infectious disease research at German universities and promote clinical research groups

Special features:

Surveillance of antibiotic consumption at 8 university hospitals and 17 regional hospitals of various sizes in

Baden-Württemberg

Limitations:

Regional study in Baden-Württemberg

Current data:

Antibiotic consumption in the inpatient sector primarily depends on a hospital's area of specialisation and less on its size; the highest antibiotic consumption rate is observed in intensive care and haematology/oncology units; increase in the consumption of reserve antibiotics; compared to other European countries, antibiotic consumption is in the lower third

Funding:

Over € 3.5 million from the BMBF for the clinical research group at the Centre for Infectious Diseases in Freiburg; funding also covers work on medical/scientific issues relating to infections, in an exchange between medical theory scientists and clinical researchers with expertise in the field of infectious diseases

GERMAPTM

Responsible:

Initiative of the German Federal Office of Consumer Protection and Food Safety (BVL), the Paul Ehrlich Society for Chemotherapy and the Freiburg Centre for Infectious Diseases

Objective:

To draw up a report on antibiotic consumption and resistance for bacterial infective agents in human and veterinary medicine in Germany (Atlas of Antibiotic Consumption and Resistance)

Special features:

Relevant specialists from various organisations and institutions (BfArM, BfT, BVL, FLI, DGHM, DGI, DVG, RKI, Freiburg Centre for Infectious Diseases) are involved; summary of the resistance and consumption situation in human and veterinary medicine in Germany

Limitations:

Incomplete data for Germany permit regional analysis for specific data only; GERMAP 2008 published in October 2008, with data up to and including 2006

European Surveillance of Antimicrobial Consumption (ESAC)^{56,121}

Responsible:

Faculty of Medicine, Microbiology Department, University of Antwerp, Belgium

Objective:

To establish a European network for the surveillance of antibiotic consumption in the outpatient sector in order to collect and assess antibiotic consumption data

Special features:

European comparative data from 34 countries for analysing trends in antibiotic consumption in the outpatient sector; feedback to participating countries

Limitations:

Data communicated by the WHO from the outpatient sector based on prescriptions charged to the statutory health insurance funds

Current data:

Antibiotic consumption in the outpatient sector in Germany is in the lower third in a European comparison; the consumption of reserve antibiotics is high in a European comparison

1.3.3 Prevention and control of antimicrobial resistance

Antimicrobial resistance can be prevented and controlled on various levels and in various areas, because numerous factors can contribute to antimicrobial resistance. On the level of prescribing antibiotics, physicians must be thoroughly familiar with the methods for diagnosing infectious diseases, the effects and dosages of antibiotics, the development of resistance and the local resistance situation, in order to make a correct diagnosis and select the right antibiotic.

Recommendations on diagnostics and therapy can help prescribing physicians make a diagnosis and select an antibiotic. Generally acknowledged national recommendations are required as a basis for elaborating local recommendations. These local recommendations take the local situation into account and frequently exist only in large hospitals in Germany. Furthermore, recommendations on hygiene and avoiding infections help to prevent the transmission and spread of (multi)resistant infective agents.

To promote the exchange of knowledge and improve communication between the various stakeholders in the health sector, networks and quality circles have been established in Germany, some of which also support the prevention and control of antimicrobial resistance, although this is frequently not their primary objective.

Public relations campaigns on the prudent use of antibiotics serve to educate both the general public and professional groups.

The section below describes activities in Germany for pre-

venting and controlling antimicrobial resistance in the following areas: recommendations, training, further education and continuing education, public relations campaigns and networks.

1.3.3.1 Recommendations

Recommendations and guidelines are decision-making aids and pointers for diagnosing and treating infections. Only in justified cases should a physician deviate from these recommendations. Guidelines are developed with the goal of improving the quality of care and treatment and increasing patient safety.

The recommendations described below are divided into the areas of diagnostics, therapy, hygiene and quality assurance. As a topic here, hygiene only includes the recommendations for preventing and controlling MRSA in hospitals and other medical facilities. All other recommendations on hygiene and infection prevention issued by the Commission on Hospital Hygiene and Infectious Disease Prevention (KRINKO) are primarily for ensuring compliance with general hygiene measures and less for preventing and controlling antimicrobial resistance. Therefore, they are not included in this section.

Because numerous recommendations exist in these areas, as elaborated by various organisations and institutions in Germany, this section presents only a selection of recommendations, mostly those relating to national and local treatment recommendations.

1.3.3.1.1 Diagnostics

S3 guidelines concerning epidemiology, diagnostics, antimicrobial treatment and management of adult patients with community acquired, deep respiratory tract infections⁷³

Responsible:

PEG, DGP, DGI, CAPNETZ Competence Network

Objective:

To establish standards for diagnosis and therapy, and promote the efficient use of antibiotics in treating community acquired pneumonia and deep respiratory tract infections

Special features:

Comprehensive guidelines covering all aspects of diagnosis and antimicrobial treatment; recommendation for the outpatient sector; implementation of the guidelines supported by the German Medical Association; evaluation of application of the guidelines shows a decline in resistance rates and in the use of broad-spectrum antibiotics

Limitations:

Must be purchased

European Committee On Antimicrobial Susceptibility Testing (EUCAST)

Responsible:

ESCMID and national commissions

Objective:

To standardise antimicrobial breakpoints (or also epidemiological limit values) and resistance testing in Europe

Special features:

Experts from all European countries collaborate to harmonise existing, national antimicrobial breakpoints; provides breakpoint tables for antibiotics and web-based software for collecting frequency distributions on the susceptibility of wild-type populations, and relevant antibiotic and pathogen combinations; subcommittees for the resistance testing of fungi and for interpreting resistance tests

Limitations:

Breakpoints are not yet available for all significant antibiotics and pathogens

1.3.3.1.2 Therapy

National recommendations on antibiotic therapy^{122,123}

Responsible:

Scientific societies

Objective:

To aid in establishing the indication for antibiotic therapy and selecting the antibiotic

Special features:

A high degree of implementation can be achieved by basing local recommendations on the national recommendations

Limitations:

Germany has no generally acknowledged, national recommendations on antibiotic therapy; the actual application of existing recommendations in Germany is unknown and has yet to be examined

Local recommendations on antibiotic therapy⁶

Responsible:

Drug commissions of clinics and hospitals, e.g. Drug Commission of Freiburg University Medical Centre

Objective:

To aid in critically establishing the indication for antibiotic therapy and selecting the antibiotic

Special features:

Recommendations drafted in collaboration with hospital directors ensure support and approval during the process of elaborating and applying the recommendations; local recommendations can be adapted to the local situation; increased patient safety; use of a uniform antibiotics regimen cuts costs in purchasing; uniform, indication-based definition of antibiotic therapy

Limitations:

Therapy geared to local recommendations is not always possible; the actual application of existing recommendations in Germany is unknown and has yet to be examined

1.3.3.1.3 Hygiene

Recommendations for preventing and controlling methicillin-resistant *Staphylococcus aureus* strains in hospitals and medical facilities¹⁰⁸

Responsible:

KRINKO

Objective:

To prevent and control methicillin-resistant *Staphylococcus aureus* strains in hospitals and other medical facilities

Special features:

KRINKO and its recommendations have a legal basis in Section 23 Para. 2 IfSG

Limitations:

Implementation of the recommendations in medical facilities, and monitoring of application by the Public Health Service (ÖGD), is frequently inadequate

1.3.3.1.4 Quality assurance

Quality standards in the microbiological diagnosis of infectious diseases (MIQ)⁸⁶

Responsible:

DGHM

Objective:

To optimise the diagnosis and therapy of infectious diseases

Special features:

Clear guidelines for a systematic approach, from a tentative clinical diagnosis, right to definitive diagnosis and therapy; complete range of laboratory diagnostics and microbiology; always up-to-date thanks to continuous updates

Limitations:

Must be purchased; extensive loose-leaf collection; the implementation and benefit of MIQ have yet to be evaluated

Guidelines of the German Medical Association on Quality Assurance in Microbiology¹³⁻¹⁵

Responsible:

German Medical Association

Objective:

Reproducibility of medical/microbiological tests

Special features:

The Professional Code for Physicians obliges them to implement measures introduced by the Medical Association to assure quality in medical practice

Limitations:

Lack of precise data on diagnostics

Quality assurance standards of the Society for Promotion of Quality Assurance in Medical Laboratories (INSTAND)⁷⁵

Responsible:

Society for Promotion of Quality Assurance in Medical Laboratories (INSTAND)

Objective:

Internal and external quality assurance and improvement of the reliability of medical/micro-biological tests

Special features:

Collaboration with various scientific/medical societies and scientific umbrella organisations, German Medical Association, etc.; offers internal and external quality assurance and mandatory testing in the field of laboratory diagnostics in accordance with the current guidelines of the German Medical Association

Limitations:

No legal basis

1.3.3.2 Basic training, specialist training and continuing education of medical occupational groups

Numerous (academic) occupations requiring formal training, as well as specialist training programmes, can be assigned to the category “medical occupational groups”. Thorough knowledge of the antimicrobial resistance problem is important for all of them.

In this context, physicians (and also dentists) who prescribe antibiotics must acquire different knowledge through their basic training, specialist training and continuing education than, for example, medical or dental

employees working in a private practice.

The topic of antimicrobial resistance must be sufficiently incorporated in basic training, specialist training and continuing education programmes for physicians to enable the correct diagnosis of infectious diseases and antibiotic therapy in line with the indications. In addition, physicians and all other medical occupational groups must have sound knowledge of the risks associated with the development of antimicrobial resistance, of general hygiene measures, infection prevention and specifically of the transmission of multiresistant infective agents.

On account of the central role physicians play, the following section covers basic training, specialist training and continuing education for this group only.

Basic medical training

The fundamentals of basic medical training are defined in Germany's Regulation on the Licensing of Doctors²⁰. Basic medical training encompasses a six-year course of study, including practical training (pre-registration year) of 48 weeks. Furthermore, medical students must complete training in first aid, a nursing internship of three months, a medical clerkship of four months and take a two-part medical examination.

The regulations governing licensing to practice medicine are standardised nationwide in the Federal Regulation on Doctors and the Regulation on the Licensing of Doctors. The Federal Ministry of Health is responsible for the content of both of these regulations.

While the Regulation on the Licensing of Doctors names only the mandatory medical disciplines, the individual universities issue specific guidelines for fulfilling all degree requirements.

Specialist medical training

Specialist medical training involves acquiring further medical knowledge or skills after having completed basic medical training and receiving a license to practice.

Specialist training is a defined process in terms of duration and content. It enables a physician to qualify as a specialist in individual disciplines and subsequently to specialise in key fields or in a supplementary specialist training programme.

The provisions regarding specialist medical training are defined in the individual Länder laws and in the autonomous articles of the State Chambers of Physicians. Consequently, they are under the jurisdiction of the 17

State Chambers of Physicians.

To support these, the German Medical Association elaborates model Regulations on Specialist Training¹⁷ for the State Chambers of Physicians, which are intended only as recommendations. However, the specialist training regulations of the Länder are frequently very similar to the model regulations issued by the German Medical Association.

Continuing medical education

All physicians are required to update and consolidate their professional skills by continuing to learn while working in their occupation. The fundamental requirement to take part in continuing education is anchored in the Professional Code for Physicians. SHI-accredited physicians and specialists in hospitals are additionally required by law to furnish proof of continuing medical education, as laid down in Book V of the German Social Security Code.

The purpose of continuing education is to impart the knowledge of medicine and medical technology required to maintain and expand competence.

Recommendations on the content of continuing medical education are formulated by the German Medical Association as follows: “Subject-specific, interdisciplinary and general knowledge, as well as training in practical skills. Topics that serve to improve social skills, communication and management skills, or knowledge of quality management and evidence-based medicine. Information relating to the health sector, as well as economic and legal topics, all of which promote occupational training for physicians, may also be included.”¹⁶

A continuing education certificate is awarded when a physician has completed continuing education programmes, within a given time period, that together add up to a specific number of points.

1.3.3.3 Networks

According to experts, the increasing problem of antimicrobial resistance is further aggravated by the lack of coordination between the stakeholders in the health sector. For example, following discharge from hospital, neither a patient's general practitioner, nor the patient himself or his relatives, are informed about an infection with a multiresistant pathogen. As a result, hygiene measures required to prevent the transmission of (multi)resistant infective agents are not carried out and the pathogen continues to spread. The problem is further aggravated because, in some cases, coverage of the costs associated

with implementing hygiene measures outside the inpatient sector is either not provided, or is unclear.

Therefore, experts recommend establishing regional networks, which they believe can make an important contribution to preventing and controlling multiresistant pathogens. This has already been demonstrated by the established MRSA-net network, and is supported by a corresponding resolution of the Conference of Ministers Responsible for Health.

EUREGIO Project MRSA-net^{31,60,92}

Responsible:

Institute of Hygiene, Münster University Hospital; Microbiology Laboratory, Twente/Enschede, NL; State Institute for the Public Health Service, North Rhine-Westphalia; Faculty of Behavioural Sciences, Twente University/Enschede, NL

Objective:

To develop a cross-border strategy for preventing and controlling MRSA in the Münsterland region of Germany and Twente/Enschede, The Netherlands, by establishing a network of all stakeholders in the health sector

Special features:

Networking of all stakeholders in the health sector; discussion, training and specialist medical training on the MRSA problem within the network; network coordinated by the public health office; cross-border cooperation and exchange of knowledge; establishment of an early-warning system for detecting unusual increases in the occurrence of specific MRSA clones; introduction of health insurance billing codes for MRSA screening and treatment in the outpatient sector

Limitations:

Restricted to the region; a sustainable structure is at risk because of limited-term financing of the project by the European Commission

Current data:

Not yet available in published form

Resolution of the 79th Conference of Ministers Responsible for Health (GMK), 30.6.2006³

Responsible:

Länder Ministries of Health

Objective:

To establish networks in all regions to reduce MRSA infections and their spread, particularly between hospitals, care homes and outpatient care facilities

Special features:

All stakeholders in the health sector (e.g. hospitals, physicians in private practice, clinical microbiologists, hygiene professionals, etc.) are to participate in the network; the network is to be coordinated by the Public Health Service; the Euregio project MRSA-net is to serve as a model for the networks to be established; the responsible ministers and senators in the Länder health systems gave their joint support to establishing these networks in the Resolution of the 79th GMK

Limitations:

The Public Health Service must be strengthened in order to implement the resolution; financing of the networks still unclear

Current data:

State of implementation unknown

Genome research on pathogenic microorganisms – PathogenoMik

Network coordinator:

University of Würzburg

Objective:

To develop strategies for controlling bacterial infectious diseases by improving diagnosis and the typing of infective agents, and by close cooperation with companies

Special features:

The BMBF's GenoMik programme has been in existence since 2001; research focuses on the pathogenic bacteria *Mycobacterium tuberculosis* and *Helicobacter pylori*; development of DNA microarrays for tuberculosis pathogens, with which a genome comparison can be made between the tuberculosis pathogen and other mycobacteria; study of *Helicobacter pylori* in 27 groups of people of different ethnic background and geographical origin

Current data:

Detailed analysis of the *Helicobacter pylori* genome showed that the bacteria can be assigned to seven groups and subgroups. These, in turn, can be traced to four *Helicobacter* populations that originated in Africa, the Middle East, Central Asia and East Asia. The *Helicobacter* types encountered in Europe today apparently result from the merging of two populations from the Middle East and Central Asia. These findings are extremely important for treatment, because genetic differences can be responsible for varying degrees of aggressiveness, and influence the efficiency of antibiotics

Outlook:

After the first two phases of funding, the network is now

to be continued within the framework of the GenoMikPlus programme, which aims to step up implementation of the research results in improved diagnosis and treatment options for bacterial diseases

PathogenoMik-Plus

Competence centres:

Universities of Bielefeld, Göttingen and Würzburg

Objective:

To continue research projects from the PathogenoMik programme that are of commercial interest and to be further developed for the market

Special features:

Alliance between companies that represent the economic interest in microbial genome research and already are involved in diverse genome research networks; establishment of an industrial platform to serve as a hub of communication on microbial genome research in Germany, not only for interested companies, but also for research organisations and political representatives

Outlook:

Plans to register as an association; funding from 2006 to 2009 encompasses a budget of some € 20 million

1.3.3.4 Public relations campaigns

Other European countries are increasingly educating the general public and medical occupational groups on aspects of antibiotic treatment and antimicrobial resistance by way of public relations campaigns, particularly countries with high antibiotic consumption in the outpatient sector, e.g. France and Belgium. For example, awareness of the effects of antibiotics was increased by advertising spots on television and radio.

In Germany, only few public relations campaigns exist at present in the field of antimicrobial resistance. Campaigns to inform physicians, like those in France that target physicians in private practice, do not exist in Germany. The most important are listed in the section below.

Antimicrobial resistance – An explosive issue⁸¹

Responsible:

Paul Ehrlich Society for Chemotherapy, German Society for Infectious Diseases, German Society for Hygiene and Microbiology

Objective:

To educate and sensitise the general public with regard to

the danger of antimicrobial resistance

Special features:

Internet campaign for the general public on the effect of antibiotics, special aspects of taking antibiotics and antimicrobial resistance; campaign office provides a hot-line for, and information on, antibiotics and resistance development

Limitations:

General public has taken little notice of the campaign

Initiative on Antibiotic Use: “Targeted is Safe” (Gezielt ist sicher)

Responsible:

Expert group for infectious diseases, pneumology and intensive therapy

Objective:

To educate professional circles and the general public regarding the targeted use of antibiotics

Special features:

Internet information campaign on the action of antibiotics, taking antibiotics, antimicrobial resistance and the diagnosis of bacterial infections

Limitations:

General public has taken little notice of the campaign

1.4 Antimicrobial resistance in an international context

1.4.1 European Commission^{27,28,97}

In 2001, the European Commission published a strategy for countering antimicrobial resistance in the Member States. The strategy includes 15 actions in the areas of surveillance, prevention, research and development, and international cooperation. One important element of the strategy is the Recommendation on the prudent use of antimicrobials in human medicine (2002/77/EC). In this Recommendation, the European Commission calls on the Member States to introduce specific strategies for the prudent use of antimicrobial agents so as to contain antimicrobial resistance.

These strategies should pursue the following primary objectives:

- a) Establishment or expansion of systems for monitoring antimicrobial resistance and the use of antibiotics

- b) Introduction of measures to control and prevent antimicrobial resistance, to promote the prudent use of antimicrobial agents and to contribute to containing infectious diseases
- c) Promotion of education and training of healthcare professionals regarding the problem of antimicrobial resistance, and information of the general public on how important it is to use antimicrobial agents prudently.

To underline the significance of the issue and support implementation of the 2003 Recommendations of the European Council on the prudent use of antimicrobial agents in human medicine, a Council Conclusion on Antimicrobial Resistance was adopted during the Slovenian Presidency of the EU Council in June 2008.⁴⁶

In addition to the Recommendations of the European Commission on the prudent use of antimicrobial agents in human medicine, projects and measures are also being funded as part of the European Framework Programmes (currently the 7th Framework Programme, FP7). The programme was launched in 2007 and will run until 2013. FP7 does not focus on the area of antimicrobial resistance.

1.4.2 European Academy Science Advisory Council (EASAC)

The EASAC is an advisory body of the European Commission, managed by the national science academies of the EU Member States. The EASAC has in recent years issued several statements on the problems of antimicrobial resistance and nosocomial infections.

1.4.3 European Centre for Disease Prevention and Control (ECDC)³⁹⁻⁴¹

Antimicrobial resistance is a high-priority issue for the ECDC. The first Annual Epidemiological Report on Communicable Diseases in Europe, published by the ECDC in June 2007, rates increasing antimicrobial resistance as one of the greatest dangers facing the EU health sector.

In its Recommendation on the prudent use of antimicrobial agents in human medicine (2002/77/EC), the European Commission calls on the ECDC to support the Commission in future in elaborating recommendations and reports on implementation of EU Recommendations by the Member States.

The ECDC primarily carries out the following activities in the area of antimicrobial resistance to help Member

States in this field:

- Coordination of surveillance networks,
- Standardisation of methods for susceptibility testing,
- Elaboration of European Recommendations on preventing and controlling infections,
- Coordination of activities in the Member States,
- Development of an Internet site with information on activities in the Member States, and
- Inspection and evaluation of activities in the Member States.

Despite the high priority of this issue at the ECDC, no apparent progress has been made with regard to implementing these activities.

1.4.4 World Health Organization (WHO)¹²⁸

The WHO published its Global Strategy for Containment of Antimicrobial Resistance in 2001. It describes antimicrobial resistance as a global problem affecting all nations around the world.

In the strategy, the WHO recommends interventions in the following areas: patients and prescribing physicians in private practice, hospitals, use in food-producing animals, health policy and health systems. These interventions are aimed at slowing the development and reducing the spread of antimicrobial resistance.

In a critical statement, the World Health Assembly (WHA) complains that the WHO Strategy for Containment of Antimicrobial Resistance has been insufficiently implemented to date. The WHA states that a globally integrated programme involving all health systems is necessary to promote efficient antibiotic use and thereby contain resistance.

1.5 Players in the field of antimicrobial resistance

This section provides a brief introduction to players who are involved in the field of antimicrobial resistance in Germany and who could potentially be interested in participating in the implementation of the strategy. They were active participants in the consultation phase. The players have a central role in elaborating, revising and implementing the strategy. While the players are assigned concrete actions in the section on national targets (Chapter

6.2), this section describes the key tasks of these players in the field of antimicrobial resistance.

Aktionsbündnis Patientensicherheit e. V. (APS – German Coalition for Patient Safety)

The German Coalition for Patient Safety works to promote safe healthcare in Germany and is committed to researching, developing and spreading the use of methods suitable for reaching this goal.

The work agenda of the German Coalition for Patient Safety encompasses a number of specific projects, which are addressed by its multidisciplinary working groups. The working groups meet regularly and publish their results in the form of recommendations, which are available free of charge to all organisations in the German health sector.

The German Coalition for Patient Safety cooperates with professional associations, scientific societies, research institutes, health insurance funds, self-administration institutions and patient organisations. It receives financial support from the Ministry of Health. International cooperation exists with sister organisations for patient safety. These cooperative efforts serve to promote scientific exchange and to prepare and implement actions and campaigns to improve patient safety in Germany.

Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften e. V. (AWMF – Association of Scientific Medical Societies in Germany)

The members of the Association of Scientific Medical Societies in Germany currently comprise 152 scientific societies in all fields of medicine.

The AWMF confers on fundamental and interdisciplinary issues and tasks, elaborates recommendations and resolutions, and actively seeks support for them from institutions involved in the field, particularly in the political sector. Apart from tackling issues of internal cooperation, which is becoming ever more urgent in view of increasing specialisation, the AWMF thus aims to more aggressively communicate the interests of medical science to external groups.

The AWMF acts by direct mandate of its member societies or through their delegates. When the AWMF addresses current problems on its own initiative, it seeks to ensure agreement with its member societies.

Arbeitsgruppe Infektionsschutz (AGI – Infection Protection Working Group)

The Infection Protection Working Group is a specialised section of the Working Group of the Supreme Health Authorities of the Federal Länder (AOLG). The AOLG and the AGI monitor and evaluate healthcare policy issues from a scientific point of view. The heads of the health departments of all the Länder and representatives of the Federal Ministry of Health (BMG) meet twice a year in the AOLG.

The AOLG handles direct preparatory work for the Meeting of the Heads of Administration of the Ministries and Senate Administrations, which in turn prepares the Conferences of Ministers Responsible for Health.

The Conference of Ministers Responsible for Health is an important body, providing a forum for an exchange of scientific and political opinion between the Ministers and Senators of Health of the Länder and of the Federal Government. It generally meets once a year and addresses all health policy issues. In addition to questions of structuring and financing statutory health insurance, the conference particularly addresses matters of preventive healthcare and safeguarding health, consumer health protection, environmental health protection, healthcare professions, drugs and addiction and European health policy. Because the Länder have their own competences in health policy, and can even influence federal projects through the Bundesrat, the Conference of Ministers Responsible for Health plays a very important role in this policy field.

Arzneimittelkommission der Deutschen Ärzteschaft (AKdÄ – Drug Commission of the German Medical Association)

The Drug Commission of the German Medical Association has the task of giving the German Medical Association independent advice on scientific issues relating to drugs. Furthermore, the Drug Commission is intended to support the Council of the German Medical Association in forming opinions on drug policy issues, and to formulate position statements on fundamental and individual issues submitted to it by the Council of the German Medical Association.

Committee on Health of the German Bundestag

The Committee on Health's sphere of responsibility essentially encompasses the portfolio of the corresponding Federal Ministry and the tasks resulting for the Federal Ministry of Health. It primarily addresses the following areas:

- Health insurance,
- Healthcare provision,

- Long-term care insurance,
- Drugs, the pharmacy sector, medical products,
- General preventive healthcare, occupations, communicable diseases, AIDS, genetic engineering,
- Prevention.

Every year, the Committee deliberates on numerous bills and motions relating to the subject areas listed above. In this connection, it regularly conducts public hearings and expert discussions to obtain a complete and largely independent picture of the subject under discussion. For this purpose, the Committee invites experts, proposed by the parliamentary groups, from all societal groups significantly affected by a given issue.

Berufsverband Deutscher Anästhesisten e. V. (BDA – Association of German Anaesthetists)

The Association of German Anaesthetists is a forum for anaesthesiologists and physicians currently receiving specialist medical training in the field of anaesthesiology.

According to its Articles of Association, the tasks of the BDA are:

- To represent this speciality within the medical community, the chambers of physicians and the Regional Associations of SHI-Accredited Physicians,
- To provide members with information on professional issues,
- To participate in all public-law tasks relating to anaesthesiology,
- To cooperate with other professional associations,
- To safeguard the sphere of responsibility of anaesthesiology, intensive care medicine, emergency medicine and pain therapy.
- Professional specialist training and continuing education in agreement with the German Society for Anaesthesiology and Intensive Care Medicine (Deutsche Gesellschaft für Anästhesiologie und Intensivmedizin e. V.).

The association further offers a number of services for its members, particularly in the area of insurance and insurance advice. In accordance with Germany's federal structure, the BDA is divided into 17 Länder associations.

Berufsverband Deutscher Hygieniker (BDH – German Association of Hygiene Specialists)

The tasks of the German Association of Hygiene Specialists include, in particular, informing the general public about the importance of the field of hygiene and environmental medicine, and distinguishing the profession of hygiene and environmental medicine specialist

from other similar professional fields by elaborating clear definitions of training and education requirements, providing political representation and harmonising the professional profile within the EU.

Bundesamt für Verbraucherschutz und Lebensmittelsicherheit (BVL – Federal Office of Consumer Protection and Food Safety)

The Federal Office of Consumer Protection and Food Safety is an independent higher federal authority dealing with market authorisation in the area of food safety and consumer protection in the portfolio of the Federal Ministry of Food, Agriculture and Consumer Protection (BMELV).

The BVL has a broad range of responsibilities, particularly:

- Reviewing applications for the registration of feed additives and coordinating the National Food Safety Management Programme,
- Registering plant protection agents and veterinary medicinal products, and cooperating on EU registration procedures in Germany,
- Ensuring the safety of registered veterinary medicinal products,
- Studying antimicrobial resistance in bacteria from food-producing animals and developing measures to avoid resistance, and
- Granting permits for releasing genetically modified organisms (GMO) for scientific experiments.

Bundesärztekammer (BÄK – German Medical Association)

The German Medical Association is the head organisation in the self-government system of the medical profession. It represents the professional policy interests of physicians in the Federal Republic of Germany. The responsibilities of the BÄK include:

- Mediating an exchange of opinions and experience between the State Chambers of Physicians,
- Maintaining contacts with the Federal Government, the Bundesrat and the political parties,
- Communicating the standpoints of the medical profession on matters of health policy and medicine,
- Promoting continuing medical education,
- Promoting quality assurance, and
- Regulating, in particular, the
- Professional code (regulating ethical and professional obligations of physicians among themselves and vis-à-vis patients), and
- Regulations on Specialist Training (defining the content, duration and objectives of specialist training and

the specialist designations).

Bundesgeschäftsstelle Qualitätssicherung (BQS – German National Institute for Quality Measurement in Health Care)

The German National Institute for Quality Measurement in Health Care has, since 2001, been managing and coordinating the development of content for, and the organisational implementation of, external, comparative quality assurance activities in German hospitals as per Section 137 of Book V of the German Social Security Code.

The mission of the BQS is to provide scientifically based statements on the quality of medical and nursing care. For example, in order to quantify, maintain and improve the quality of hospital care, the BQS has access to data on about 20 percent of all inpatient treatment cases in German hospitals. This source of data supports analyses and evaluations that can be put to diverse uses.

Through the Act to Strengthen Competition in the SHI System, the Federal Joint Committee is now obliged in future to assign quality assurance tasks, previously given to the German National Institute for Quality Measurement in Health Care, to a new, independent institution (to be selected in a competitive process). This institution is scheduled to take up its work in 2009.

Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM – Federal Institute for Drugs and Medical Devices)

The Federal Institute for Drugs and Medical Devices is an independent higher federal authority in the portfolio of the BMG.

One of the primary tasks of the BfArM is to deal with marketing authorisations, and the extension of authorisations, for finished drugs on the basis of the German Drug Law. It reviews the proof provided of a product's efficacy, safety and suitable pharmaceutical quality. When it comes to antibiotics, the most critical aspect is assessing efficacy and safety. The BfArM's Pharmacovigilance Department is additionally responsible for the safety of drugs after marketing authorisation. Reports on adverse drug reactions are collected and analysed in order to initiate steps towards risk minimisation as necessary.

Bundesinstitut für Risikobewertung (BfR – Federal Institute for Risk Assessment)

As a higher federal authority in the portfolio of the Federal Ministry of Food, Agriculture and Consumer Protection (BMELV), the Federal Institute for Risk Assessment is responsible for the safety of foods, substances and products, and thus for consumer protection.

The BfR elaborates health assessments and action options for government agencies responsible for risk management. The work results and recommendations of the BfR serve all interested groups as key decision-making aids for various programmes. With its science-based risk assessments, the BfR plays a leading role in consumer health protection in Germany and abroad.

In addition, it has the statutory task of providing information on potential, identified and assessed risks that foods, substances and products pose for consumers. The entire assessment process is presented in such a way that it is easily understood by the general public. By way of comprehensive and comprehensible risk communication, the BfR makes science visible and useful to consumers.

Bundesministerium für Bildung und Forschung (BMBF – Federal Ministry of Education and Research)

The BMBF activities in health research are characterised by a comprehensive approach, ranging from studying the cause of disease and preventive healthcare, to structural changes in research, all the way to improved cooperation between the economy and science. Researching the causes and development of diseases, instead of simply controlling symptoms, is a key objective of BMBF funding. In this context, it is important for physicians, researchers, hospitals and private practices in various special disciplines to collaborate on research. Furthermore, another objective is to exploit existing or underdeveloped potentials in biomedical research for the purpose of effective diagnosis and therapy. For example, functional human genome research, in particular, is expected to deliver valuable findings for controlling diseases.

Current and planned funding programmes are coordinated and networked with the relevant action plans of the European Union's 6th and 7th Research Framework Programmes. In addition, the 6th and 7th EU Research Framework Programmes offer an opportunity to establish topically focused networks with representatives of research promotion and programme development (European Research Area Networks, ERA-NET). The goal of these networks is to efficiently harmonise the respective national programmes and implement a joint European programme, initiated by the national funding organisations.

Over the last three years (2005–2007), the Federal Ministry of Education and Research has invested over € 320 million in health research, in addition to over € 175 million for implementing the “National Genome Research Network: Controlling Disease through Genome Research”. A total of € 141.6 million is to be invested in 2008 to fund projects in the programme, “Health Research: Scientific Research for People”.

The BMBF has been funding infection research since 1981. The objective of funding is to pool existing research potentials and to promote targeted development in such a way that scientific progress can benefit patients as quickly as possible. Scientific results are to be implemented directly in therapeutic and diagnostic measures. At present, some € 20 million a year are invested to promote projects.

The following key areas are funded:

- **Clinical Infectiology:** to support clinical research into infectious diseases in Germany and build a bridge between research and clinical practice.
- **Product-Oriented Vaccine Development:** for the targeted improvement of candidate vaccines.
- **Medical Competence Networks on Infectious and Inflammatory Diseases:** including hepatitis, sepsis, HIV/AIDS and community acquired pneumonia; to improve the transfer of results from basic research to clinical research and finally to patient care.
- **Research Networks on Susceptibility and Resistance to Infections:** to identify the significance of related mechanisms in order to develop new approaches to disease-based research and new treatment strategies.
- **Zoonotic Infectious Diseases (zoonoses):** to strengthen cooperation between human and veterinary medicine, in particular.
- **TSE (transmissible spongiform encephalopathies):** research and development to improve diagnostic methods and treatment options.
- **National Genome Research Network (NGFN):** with the disease-oriented “Infections and Inflammations” genome network.
- **Pathogenomics:** for research into specific microorganisms.
- **GenoMik and GenoMik-Plus programme:** exploiting the potential of microorganisms through global, genome-based research strategies.

Bundesministerium für Ernährung, Landwirtschaft und Verbraucherschutz (BMELV – Federal Ministry of Food,

Agriculture and Consumer Protection)

The Federal Ministry of Food, Agriculture and Consumer Protection is responsible for ensuring food safety, while safeguarding economic sustainability for producers in the agricultural sector and maintaining ecologically and socially intact rural regions. The Ministry's portfolio includes seven Research Centres, the BfR and the BVL. The primary tasks of the Research Centres is to elaborate science-based decision-making aids for food, agriculture and consumer protection policy for the Federal Government. At the same time, their findings benefit both the common good and consumers.

**Bundesministerium für Gesundheit
(BMG – Federal Ministry of Health)**

The Federal Ministry of Health is responsible for a variety of policy fields, whereby its activities focus on the drafting of bills of law, ordinances and administrative regulations.

One of its key tasks is maintaining, securing and further developing the capacity of statutory health insurance and long-term care insurance.

The reform of the health sector is one of the Ministry's most important tasks. The objective is to further develop the quality of the health sector, bolster the interests of patients, ensure cost-efficiency and stabilise contribution rates.

Some of the Ministry's priority areas in the health sector are prevention, health protection, disease control and biomedicine. By means of the Protection Against Infection Act, prevention, counselling and personal responsibility in the prevention of infection are clearly emphasised and the public healthcare system strengthened. The Transplantation Act, the Protection of Embryos Act and the Stem Cell Act establish the regulatory framework for these important fields of medicine.

The Federal Ministry of Health also draws up the framework provisions governing the manufacture, clinical trial, marketing authorisation, distribution channels and surveillance of medicinal products and medical devices, so as to fulfil the existing high requirements in terms of quality, effectiveness and safety. A core long-term task of the Ministry and its subordinate authorities is the safety of biological medicinal products, such as blood products. In addition, the Federal Ministry of Health supports research and facilitates the creation of new care provision structures. This applies, for example, in the case of mental health, assistance to the chronically ill, child health and the counselling and care of persons infected with HIV or suffering

from AIDS. In order to continually improve the level of knowledge with respect to the healthcare system, the necessary information is collated within the framework of Germany's health monitoring system.

The prevention of drug and addiction risks forms part of disease control and, as such, constitutes a central area of this Ministry's sphere of responsibility.

The profession-related legislation governing licensing to practise those medical and health professions which are regulated by federal law – including the corresponding training regulations – the aim of which is to ensure the quality of training in the health professions and therefore, also, the quality of medical and nursing care, similarly falls within the scope of the Ministry's responsibilities.

Alongside national health policy, European and international health policy also form part of the Federal Ministry's portfolio. Globalisation, tourist traffic, the opening towards our neighbours in Eastern Europe, all lead to a situation where new risks and dangers prematurely thought to be overcome, have to be countered jointly with partners wherever they emerge.

Also assigned to the Ministry are the Federal Government's Drug Commissioner and the Federal Government Commissioner for Patients' Affairs.

Bundesministerium für Umweltschutz, Naturschutz und Reaktorsicherheit (BMU – Federal Ministry for the Environment, Nature Conservation and Nuclear Safety)

The Federal Ministry for the Environment, Nature Conservation and Nuclear Safety centrally coordinates environmental policy on behalf of the German Federal Government.

The Basic Law gives rise to three different levels of legislative competence in international and EU affairs for the Federal Government and thus for the BMU:

- For environmental protection treaties with other states or international organisations,
- For the areas of water management, nature protection, rural conservation and regional planning,
- For the areas of waste management, air pollution control, noise control, nuclear energy, radiation protection and chemical safety, subject to competitive legislative competence.

Bundestierärztekammer (BTK – German Veterinary Association)

The German Veterinary Association is the nationwide rep-

representative of the members of all veterinary professions. The tasks of the BTK are:

- To ensure a continuous exchange of experience among the State Chambers of Veterinaries, jointly coordinate objectives and activities, promote the most uniform possible regulation of professional codes governing veterinaries and the principles of practicing veterinary medicine,
- To advise the State Chambers of Veterinaries,
- To represent the interests of veterinaries vis-à-vis legislators, government administrative bodies and the general public,
- To promote continuing education (particularly by funding the Academy of Continuing Education in Veterinary Medicine), as well as basic and specialist training,
- To represent the professional interests of veterinaries on the national and international level.

Bundesverband der Arzneimittel-Hersteller e. V. (BAH – Federal Association of Pharmaceutical Manufacturers)

The Federal Association of Pharmaceutical Manufacturers represents the political interests of pharmaceutical manufacturers vis-à-vis the Federal Government, the Bundestag and the Bundesrat. The association is committed to the interests of pharmaceutical manufacturers, actively helping to shape health policy issues and closely following relevant legislative processes. It is responsible on the one hand for formulating position statements in the interests of the member companies, and on the other hand for supporting the political decision-making process in view of its overall political obligation, this resulting from its factual and technical competence in questions relating to the pharmaceuticals and the health system, the aim being to bring about decisions that are effective and a benefit to consumers. Therefore, technical discussions in preparation for draft legislation make up a great part of the association's work.

Another natural focus of the association's work is to provide member companies with comprehensive advice and rapid information. Apart from the political activities of the BAH, the association's activities are characterised by basic scientific work in the pharmaceutical sector in a broad range of areas. Information on pharmaceuticals is collected and analysed in order to formulate position statements on occurrences in the pharmaceutical sector.

Bundesverband der Ärzte des öffentlichen Gesundheitsdienstes (BVÖGD – Federal Association of Public Health Service Physicians)

The Federal Association of Public Health Service Physicians is the umbrella organisation of all the State Associations of Public Health Service Physicians represented in the Länder. The BVÖGD represents the professional/political interests of this group on the state and federal levels.

The Federal Association is represented in bodies of the German Medical Association and is a member of the Committee for Physicians in Public Service and the Committee for Health and Environment. It is a member of the umbrella organisation “Deutsche Gesellschaft für Public Health e. V.” (DGPH – German Society for Public Health), the European Union for School and University Health and Medicine (EUSUHM) and the World Federation of Public Health Associations (WFPHA).

Berufsverband der Ärzte für Mikrobiologie und Infektionsepidemiologie (BÄMI – Federal Association of Doctors for Microbiology and Infection Epidemiology)

The association represents all professional interests of its members in the areas of medical microbiology, infection epidemiology, infectious disease research and hospital hygiene. This includes, in particular: representing the economic interests of the members vis-à-vis government agencies, State Chambers of Physicians, Regional Associations of SHI-Accredited Physicians and other associations and organisations; promoting, preparing and implementing continuing education and specialist training events on the national and European level; and advising the members and representing them in the respective bodies on issues relating to the quality of services to be rendered and how to safeguard this quality.

Bundesverband für Tiergesundheit e. V. (BfT – Federal Association for Animal Health)

As the representative of the animal health industry in Germany, the BfT is committed to the well-being of both animals and people. This means maintaining the health of farm and hobby animals and securing healthy food in the long-term, but also pursuing sustainable environmental protection. Based on these principles, the association's mission in Germany is to:

- Represent member interests vis-à-vis legislators, government agencies and professional organisations,
- Support high standards in maintaining animal health and in the entire food production chain, and
- Inform the general public about animal health and animal health products in order to strengthen confidence in the industry's actions and products.

Bundesverband praktizierender Tierärzte (bpt – Federal Association of Practising Veterinaries)

The association's mission is to promote the professional, economic and social interests of its members in the Federal Republic of Germany.

It pursues the following objectives:

- Independence of practising veterinaries and their profession,
- Securing of a decisive influence of veterinaries on all institutions involved in animal health,
- Exploitation of all advances in science, maintenance and improvement of the health of house pets,
- Promotion of animal protection,
- Protection of people against the risks arising from keeping pets and livestock.

Bundesvereinigung Deutscher Apothekerverbände (ABDA – Federal Union of German Associations of Pharmacists)

The Federal Union of German Associations of Pharmacists is the head organisation of pharmacists in Germany. The aim of the association is to represent and promote the common interests of this healthcare profession. The member organisations of the ABDA are the 17 Councils of Pharmacists and the 17 Associations of Pharmacists at the state level. The Councils of Pharmacists are united in the National Council of Pharmacists; the Associations of Pharmacists are part of the German Pharmacists' Association. To promote the interests of its members, the ABDA provides a basis for an intensive exchange of opinion between its 34 member organisations. It advises them on all processes in the healthcare and pharmaceutical sector. The ABDA negotiates all issues of national importance with the institutions, authorities, corporations, etc. that deal with questions of pharmaceutical distribution. Furthermore, the head organisation maintains constant contact with the pharmaceutical science community in Germany and abroad.

Bundeszahnärztekammer – Arbeitsgemeinschaft der deutschen Zahnärztekammern e. V. (BZÄK – German Dental Association)

The German Dental Association represents the professional interests of all dentists in Germany at the federal level. The members of the BZÄK are the State Chambers of Dentists, which send delegates to the Federal Assembly, the supreme decision-making body of the German Dental Association. The Presidents of the State Chambers of Dentists, together with the President and Vice Presidents of the BZÄK, form the Council.

The German Dental Association represents the interests of dentists relating to health policy and professional issues. Its chief mission is to strive for a liberal, future-oriented healthcare system with the patient at the centre of its efforts in dental medicine, in which the dentist/patient relationship can develop without any outside influence.

Bundeszentrale für gesundheitliche Aufklärung (BZgA – Federal Centre for Health Education)

As a specialist agency in the portfolio of the BMG, the Federal Centre for Health Education is responsible at the national level for providing health education to promote the interests of government health policy. The core tasks of the BZgA's health education activities are to:

- Elaborate principles and guidelines for the content and methods of practical health education,
- Provide training and continuing education for people active in the field of health education,
- Coordinate and strengthen health education in the Federal Republic of Germany,
- Cooperate with international organisations on these core tasks.

Preventive healthcare and maintaining good health are the two primary objectives of the BZgA. In this context, the focus is on promoting the willingness of individuals to adopt responsible, healthy lifestyles and to make proper use of the health system.

Codex Alimentarius Commission

The Codex Alimentarius Commission is a partnership between WHO and FAO for addressing interdisciplinary issues. The Codex Alimentarius Commission was established in 1963 to develop food recommendations, standards and guidelines (e.g. codes of practice under the Joint FAO/WHO Food Standards Programme). The main purposes of the Codex Commission are to protect the health of consumers and ensure food safety. An Ad Hoc Intergovernmental Task Force on Antimicrobial Resistance (TFAMR) was created within the Codex Commission to address the problem of antimicrobial resistance. For example, the task force is to pursue the question as to what degree cross-border food transports promote the spread of resistances.

Deutsche Forschungsgemeinschaft (DFG – German Research Foundation)

The German Research Foundation is the largest research

promotion organisation in Germany with a total budget of some € 2 billion. The DFG funds projects in all fields of science, with 90 % of all funding going to universities. Numerous studies on antimicrobial resistance, microbial pathogenesis and the molecular basis of infectious diseases have received funding in the framework of DFG projects. Competent scientists from German research organisations are represented in the Specialist Working Group for Microbiology, Virology and Immunology.

Deutsche Gesellschaft für Anästhesiologie und Intensivmedizin e. V. (DGAI - German Society for Anaesthesiology and Intensive Care Medicine)

The German Society for Anaesthesiology and Intensive Care Medicine is a medical scientific society. According to its Articles of Association, its tasks are to:

“... provide a forum for physicians to join forces in expanding and advancing anaesthesiology, intensive care medicine, emergency medicine and pain medicine, and to ensure the best possible care of the general population in these areas”. The DGAI is a member of the World Federation of Societies of Anaesthesiologists (WFSA). In accordance with Germany's federal structure, the DGAI is divided into 17 Länder associations, which offer regional continuing education programmes.

Deutsche Gesellschaft für Hygiene und Mikrobiologie (DGHM – German Society for Hygiene and Microbiology)

The German Society for Hygiene and Microbiology is a scientific society that strives to bring together all scientists active in the field of microbiology and hygiene in Germany. The DGHM's mission is to promote research and teaching in the various areas of microbiology, infection immunology and hygiene, as well as in the health system, by initiating an exchange of scientific and practical experience, holding scientific events and carrying out joint scientific projects.

Deutsche Gesellschaft für Infektiologie (DGI – German Society for Infectious Diseases)

The German Society for Infectious Diseases is a scientific society representing the field of infectious disease in human medicine in hospitals, practices and research. The interdisciplinary nature of infectious disease medicine is emphasised by recruiting members of the DGI from various fields and sub-fields of medicine and by implementing interdisciplinary continuing education events and congresses.

In the science community, the DGI strives to establish interdisciplinary cooperation between the basic clinical and theoretical subject areas. In doing so, an effort also is

made to network with other disciplines and scientific societies that are not primarily active in the field of infectious disease. Sections are formed to jointly study core topics of common interest.

Deutsche Gesellschaft für Krankenhaushygiene (DGKH – German Society for Hospital Hygiene)

The German Society for Hospital Hygiene strives to prevent and control hospital-acquired and practice-acquired infections, focusing on infection prophylaxis, health promotion and environmental protection.

The tasks of the DGKH include cooperating with all medical and technical disciplines, economists, lawyers, human biologists and architects; elaborating clear, scientifically based recommendations; formulating position statements on current issues; and organising congresses, specialist conferences and specialist training programmes.

Deutsche Krankenhausgesellschaft (DKG – German Hospital Federation)

The German Hospital Federation unites the national and state associations of hospital owners/operators. It supports its members in fulfilling their tasks and in the hospital system. In cooperation with government and other institutions in the health sector, the DKG helps to maintain and improve the performance of hospitals. It additionally cultivates and promotes an exchange of experience and supports scientific research on the health sector. It addresses basic issues affecting not only individual national and state associations, informs the general public and supports government bodies and agencies in preparing and implementing laws. The DKG further represents the interests of the German hospital sector in European and international associations.

Deutscher Bauernverband (DBV – German Farmers Association)

The German Farmers Association represents the interests of agriculture and forestry in Germany. Founded in 1948, the German Farmers Association is the first grouping of its kind in the history of German agriculture to provide for the uniform, independent and self-determined representation of farming families and their professional interests.

The DBV

- Champions the concerns of its members at all political levels. The same applies to the European level, through membership of the European Committee of Professional Agricultural Organisations (COPA),
- As a competent representative, provides information

to politicians, the media and the general public, giving them an authentic picture of the economic and social situation of farmers and of current issues in agricultural policy and markets,

- As a service-provider, offers its member numerous services and exclusive information, and supports farmers in managing their businesses and dealing with government agencies.

Deutscher Pflegerat e. V. (DPR – German Nursing Council)

As a national working group of nursing organisations, the German Nursing Council partners with the head associations of the self-governing bodies and represents the interests of the nursing and midwifery sector in Germany. The DPR aims to coordinate the positions of nursing organisations and manage their political assertion.

Deutsches Institut für Medizinische Dokumentation und Information (DIMDI – German Institute of Medical Documentation and Information)

The German Institute of Medical Documentation and Information is an agency within the sphere of the BMG that makes information from the entire field of medicine available to the professionally interested public.

DIMDI's tasks essentially encompass three areas:

- Providing information from the entire field of medicine and related areas,
- Establishing and operating database-assisted information systems for drugs and medical devices and publishing official classifications within the framework of its statutory tasks,
- Collecting documentation and establishing a database-assisted information system for the health economics evaluation of medical methods and technologies.

Deutsche Veterinärmedizinische Gesellschaft (DVG – German Society for Veterinary Medicine)

The German Society for Veterinary Medicine is a scientific society committed to veterinary medicine. Its sphere of responsibilities includes: promoting science, research and teaching; promoting junior professionals; organising scientific congresses for continuing education in all areas of the veterinary profession; and serving as an advisory body to the general public, the media, and politics.

European Food Safety Authority (EFSA)

The European Food Safety Authority is the keystone of European Union (EU) risk assessment regarding food and feed safety. In close collaboration with national authori-

ties and in open consultation with affected stakeholders, the EFSA provides independent scientific advice and clear communication on existing and emerging risks.

In late 2005, the EFSA published its first annual report on infectious diseases transmissible from animals to humans (zoonoses). At the request of the Council of Ministers of the European Union (EU), the EFSA has now for the first time set out a series of scientific conclusions and recommendations, as well as risk communication initiatives, to prevent and reduce zoonotic diseases in the EU. The Authority has also identified aspects of the zoonosis reporting system that need to be improved.

European Commission (EU)

The European Commission is an organ of the European Community. In accordance with the EU Treaty, measures of the EU must aim to improve public health, prevent diseases and epidemics and identify risks to human health. The Health Strategy of the EU primarily focuses on strengthening cooperation and coordination, promoting an exchange of sound information and scientific findings, and supporting the decision-making process at the national level. For this purpose, the EU is developing a comprehensive health information system designed to provide EU-wide access to reliable and current information on key issues in the health sector. Furthermore, it promotes epidemiological surveillance and the control of infectious diseases. Other objectives of the strategy include ensuring patient safety and the quality of health-care in order to facilitate cross-border healthcare and the mobility of both employees and patients in the health system.

European Centre for Prevention and Disease Control (ECDC)

The European Centre for Prevention and Disease Control's mission is to strengthen Europe's defences against infectious diseases. The Centre has only few staff members, but a large network of partners in the EU, and in the EEA and EFTA Member States. ECDC works in partnership with national health authorities across Europe to strengthen and develop continent-wide disease surveillance and early-warning systems. Through such collaboration, ECDC pools Europe's health knowledge, so as to develop authoritative scientific opinions about the risks posed by current and emerging infectious diseases.

The Centre's tasks include:

- Expanding capacities within the Community and the individual Member States to protect human health by way of corresponding measures for preventing and

controlling diseases,

- Independent actions, if the Community is threatened by the outbreak of infectious diseases of unknown origin,
- Implementation of additional, coherent measures in the area of public health, by pooling the tasks and spheres of responsibility of the Member States, the institutions of the EU and leading international organisations.

Food and Agriculture Organization of the United Nations (FAO)

The Food and Agriculture Organization's mandate is to improve the production and distribution of agricultural products, particularly food, around the world, the aim being to secure a healthy food supply and improve standards of living. To this end, FAO developed the Codex Alimentarius, for example, which defines international standards for food safety. FAO essentially focuses on four areas:

- Development assistance,
- Information on nutrition, food, agriculture, forestry and fishery,
- Advice to governments,
- International forum on major food issues.

Friedrich Loeffler Institute (FLI)

The Friedrich Loeffler Institute is an independent higher federal authority in the portfolio of the Federal Ministry for Food, Agriculture and Consumer Protection (BMELV). The main tasks of the FLI include:

- Researching infectious diseases in livestock and related sciences,
- Fulfilling tasks assigned under the Animal Diseases Act,
- Publishing research results,
- National and international cooperation with scientific experts and institutions.

Gemeinsamer Bundesausschuss (G-BA – Federal Joint Committee)

The Federal Joint Committee is the highest decision-making body in the joint self-governing system for physicians, dentists, psychotherapists, hospitals and statutory health insurance funds in Germany. In the form of directives, it defines the services of the statutory health insurance system for more than 70 million insureds, thereby determining which medical care services are covered by statutory health insurance. Furthermore, the G-BA adopts quality assurance measures for the outpatient and inpatient sectors of the healthcare system. The G-BA is supervised by

the BMG. However, the G-BA is an independent legal entity under public law.

Gemeinsamer Wissenschaftlicher Beirat (GWB – Joint Scientific Advisory Board)

The Joint Scientific Advisory Board serves to provide independent advice on all science and research issues to the Federal Ministry of Health and all institutions in its portfolio: the Federal Centre for Health Education, the German Institute of Medical Documentation and Information, the Paul Ehrlich Institute, the Federal Institute for Drugs and Medical Devices and the Robert Koch Institute.

The establishment of the GWB is based on a resolution adopted by the German Bundestag on 28 April 1994 in connection with the passing of the Act on the Restructuring of Central Public Health Institutes. It provides for the establishment of an interinstitutional scientific advisory board to promote cooperation in science and research between the BMG and all institutions in its portfolio.

The ten members of the GWB are the chairmen of the individual advisory boards of the respective institutions and the directors of the institutions in the portfolio; permanent guests are the deputy chairmen of the individual advisory boards of the respective institutions.

Gemeinschaft Fachärztlicher Berufsverbände (GFB – Federation of Professional Associations of Medical Specialists)

The Federation of Professional Associations of Medical Specialists is the umbrella organisation of the professional associations of medical specialists in Germany. It represents over 100,000 members within its 27 affiliated associations, making it the largest, independent medical professional representation group in Germany, after the German Medical Association and the National Association of SHI-Accredited Physicians (KBV), which, however, are statutory bodies subject to government supervision.

Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (IQWiG – Institute for Quality and Efficiency in Health Care)

The Institute for Quality and Efficiency in Health Care is an independent scientific institute that studies the benefits and risks of medical interventions for patients, by evaluating quality and efficiency. The Institute investigates what therapeutic and diagnostic services are feasible and meaningful, and communicates its findings to the Federal Joint Committee for its decisions.

It was established as an institution of the Foundation for

Quality and Efficiency in Health Care (Stiftung für Qualität und Wirtschaftlichkeit im Gesundheitswesen) to work on behalf of the Federal Joint Committee and the Federal Ministry of Health. The IQWiG is financed by surcharges on inpatient and outpatient healthcare services, most of which are reimbursed by the statutory health insurance funds (GKV).

The institute works to evaluate diagnostic and treatment methods, medicinal products and treatment guidelines, and to provide health information to the general public. Following the principles of evidence-based medicine, the IQWiG also formulates recommendations for treatment programmes for the chronically ill, tailored to DMP (Disease Management Programmes). In this way, the institute contributes to improving healthcare in Germany.

Kassenärztliche Bundesvereinigung (KBV – National Association of SHI-Accredited Physicians)

The National Association of SHI-Accredited Physicians represents the political interests of SHI-accredited physicians and psychotherapists in private practice. It is supervised by the Federal Ministry of Health and voices the concerns of its members to the German Federal Government in legislative procedures. The statutory tasks of the association include asserting the rights of physicians in private practice vis-à-vis the health insurance funds, as well as safeguarding and ensuring the provision of healthcare by SHI-accredited physicians and psychotherapists. As a body within the medical self-government system, the KBV concludes contracts with the head associations of the statutory health insurance funds and other providers of social security benefits. Further, together with the health insurance funds, the KBV defines the nationwide fee scale for physicians in private practice, the so-called “Uniform Assessment Standard”, and negotiates criteria for distributing the total remuneration for medical services by care sectors. In the Joint Federal Committee, the KBV collaborates with representatives of the health insurance funds to define statutory health insurance benefits. The KBV provides information and support for the Regional Associations of SHI-Accredited Physicians on all issues in its sphere of responsibility. It also advises legislators in the area of healthcare policy.

Landesärztekammern (State Chambers of Physicians)

In the Länder of the Federal Republic of Germany, the State Chambers of Physicians are responsible for representing the professional interests of physicians. This includes, above all, regulating medical practice and organising the medical profession. Because two State Chambers of Physicians were formed in North Rhine-West-

phalia to serve the two regions of the state, there are a total of 17 State Chambers of Physicians today, all being legal entities under public law.

Landestierärztekammern (State Chambers of Veterinaries)

Similar to the State Chambers of Physicians (see above), the State Chambers of Veterinaries are responsible for representing the professional interests of veterinaries. Because two State Chambers of Veterinaries were formed in North Rhine-Westphalia to serve the two regions of the state, there are a total of 17 State Chambers of Veterinaries today.

Medizinische Fakultätentag (MFT – Medical Faculty Association)

The Medical Faculty Association is a conference of medical education and research institutions at universities that are members of the German University Presidents Conference.

The goals of the MFT are to support autonomous and independent research and teaching in medicine, and to responsibly provide state-of-the-art healthcare to patients at university medical centres.

The mission of the MFT is to:

- Represent the specialist interests of medical faculties in public and thereby serve as a point of contact for politicians and government administrators,
- Provide framework conditions ensuring that medical/dental educational institutions are able to fulfil their tasks in research and teaching,
- Promote specialist training and continuing education in medical fields, insofar as this jointly concerns all members, without affecting the tasks of the scientific societies and the bodies representing the professional interests of physicians,
- Advise members, and represent their common interests, in the fields of medical/dental teaching and medical research,
- Promote an exchange of information and experience among members,
- Contribute to the medical/dental care of the general population by advising government agencies, organisations, associations and representative bodies.

Nationale Referenzzentren und Konsiliarlaboratorien (NRZ – National Reference Centres and Consultant laboratories)

National Reference Centres for the surveillance of critical

infective agents are appointed by the Federal Ministry of Health. In each case, appointments are made for a period of three years, in consultation with representatives of the Robert Koch Institute, the Commission for Infection Epidemiology and the medical/scientific societies. In making decisions regarding the appointment of reference centres, consideration is given to the epidemiological relevance of pathogens and special diagnostics, as well as questions of resistance and measures for infection protection.

To have access to specialist advice for the broadest possible range of pathogens, consultant laboratories also are appointed for the same time period for additional infective agents relevant to health and for pathogenic, clinical syndromes of particular significance in terms of infection epidemiology. They are recommended by the scientific societies and then appointed by the RKI after a consensus is reached with representatives of the BMG, the RKI and the Commission for Infection Epidemiology.

Nationales Referenzlabor für Antibiotika-Resistenz (NRL-AR – National Reference Laboratory for Antimicrobial Resistance)

The National Reference Laboratory for Antimicrobial Resistance was transferred from the BMELV to the Federal Institute for Risk Assessment (BfR) in accordance with Section 33 of Regulation (EC) 882/2004. The primary mission of the NRL-AR is to achieve high quality and uniform test results.

Its work focuses on collecting comparable data on antimicrobial resistance in zoonotic agents and other pathogens, insofar as they pose a threat to public health. To this end, the NRL-AR coordinates the choice of isolates for testing together with the Länder and their laboratories, while also conducting its own resistance tests on isolates originating from animals, food, feed and the environment. The results are compiled regularly in the Annual Zoonosis Report, which is drawn up for Germany in accordance with Article 9 of Directive 2003/99/EC and submitted to the European Food Safety Authority (EFSA).

Öffentlicher Gesundheitsdienst (ÖGD – Public Health Service)

The Public Health Service is an organisation of service agencies on the federal, state, district and municipal levels, all of which work to protect the health of the general public and the individual. The tasks of the Public Health Service are not regulated uniformly in Germany. Despite the different statutory regulations in the Länder, the fundamental character of the tasks handled by the Public Health Service are the same. Essentially, the agencies of

the Public Health Service promote and protect the health of the general public. In doing so, they cooperate with other providers, institutions and associations active in health-related fields.

The Public Health Service's local agencies are the "Gesundheitsämter", or public health offices. Germany has both state (e.g. at the administrative district offices in Baden-Württemberg) and municipal health offices or health agencies. The tasks of the local public health offices vary from one state to the next. Core responsibilities include: monitoring hygiene in various institutions, such as hospitals and water supply plants; physical examinations for children starting school; support for addicts; health-related information, education and advice for the general public; and support for health-related self-help groups.

The work of the local health offices is anchored in law in the Länder Health Acts and in federal regulations, such as the Protection Against Infection Act and the Drinking Water Ordinance.

Spitzenverband Bund der Krankenkassen (Central Federal Association of Health Insurance Funds)

The Central Federal Association of Health Insurance Funds represents the interests of statutory health insurance (GKV) at the federal level and regulates the framework conditions for promoting greater competition regarding the quality and efficiency of healthcare. The agreements concluded by the Central Federal Association of Health Insurance Funds, and its other decisions, apply to the members of the Central Federal Association, the Länder associations of the statutory health insurance funds, and the insureds.

The Central Federal Association of Health Insurance Funds supports the health insurance funds and their Länder associations in fulfilling their tasks and representing their interests.

The Central Federal Association of Health Insurance Funds formulates recommendations for the appointment and distribution of the commissioned agencies in order to ensure nationally uniform collection practices.

The Central Federal Association of Health Insurance Funds is an entity under public law and subject to the supervision of the Federal Ministry of Health. The Supervisory Board of the Central Federal Association of Health Insurance Funds comprises insured and employer representatives from the local health insurance funds, substitute health insurance funds, works health insurance funds,

guild health insurance funds, the Seamen's Health Insurance Fund, the German Pension Insurance Fund for Miners, Railway Workers and Seamen, and agricultural health insurance funds.

Paul-Ehrlich-Gesellschaft für Chemotherapie e. V. (PEG – Paul Ehrlich Society for Chemotherapy)

The Paul Ehrlich Society is a German-speaking scientific society in the field of chemotherapy. It strives to unite all physicians, veterinaries and natural scientists interested in chemotherapy, its fundamentals and its application, as well as groups that support these interests. The society further aims to promote research and teaching in the fields mentioned by encouraging an exchange of experience, holding scientific events and conducting joint scientific studies.

Projektträger des Deutschen Zentrums für Luft- und Raumfahrt (PT-DLR – Project Management Agency of the German Aerospace Centre)

The Project Management Agency of the German Aerospace Centre is a research funding organisation supporting the Federal Ministry of Education and Research, the Federal Ministry of Economics and Technology and the Federal Ministry of Health in the scientific and organisational implementation of programme-related project funding, making it an indispensable part of the project funding systems of these ministries.

Various sections of the PT-DLR are also involved in promoting health research, which has been a main area of the PT-DLR's work for many years (PT-DLR GF).

Robert Koch Institute (RKI)

The Robert Koch Institute is a federal institution in the portfolio of the Federal Ministry of Health. The RKI is the central federal institution responsible for disease control and prevention and is therefore the central federal reference institution for both applied and response-oriented biomedical research. The RKI's mission is to identify, prevent and control diseases, particularly infectious diseases. It is required by law to elaborate scientific findings as a basis for making health policy decisions. Primary tasks include the scientific study, epidemiological and medical analysis and assessment of diseases that are highly dangerous, display widespread prevalence or are significant to the general public or health policy. The RKI advises the responsible federal ministries, particularly the BMG, and helps to develop standards. It informs and advises the professional public and increasingly also the general public. With regard to identifying health hazards and risks, the RKI plays a central role by providing an early-warning system.

Universities / Academic Research Institutes / Science Academies

Universities are scientific institutions of higher education that represent the sciences in research, teaching, degree-level study and training, teach subjects systematically and give students access to coursework and occupational qualifications of the highest standard in their sphere of validity. The Science Academies regularly publish position papers on a variety of issues. Leopoldina (German Academy of Sciences) and the European Academy Science Advisory Council (EASAC) recently elaborated key position statements on infectious disease and the antimicrobial resistance problem.

Verband der Leitenden Krankenhausärzte Deutschlands e. V. (VLK – Association of Senior Hospital Physicians in Germany)

The Association of Senior Hospital Physicians in Germany is the union of all senior physicians in hospitals. The association's mission is to actively participate in shaping and maintaining an efficient, functioning and patient-oriented hospital system.

To achieve this goal, the association promotes an intense exchange of opinion and experience among its members in all 16 Länder associations. It incorporates the ideas and experiences acquired in this way into its regular meetings with key organisations, institutions and persons active in the health sector, and represents the interests of senior hospital physicians in the political and health policy sector, as well as in public.

Verband der niedergelassenen Ärzte Deutschlands (NAV-Virchow-Bund – Association of Physicians in Private Practice in Germany)

The Association of Physicians in Private Practice in Germany represents the interests of all physicians in all specialty fields who want to go into private practice, are in private practice or who work in the outpatient sector, vis-à-vis the Federal Government, parliament, the medical and non-medical public, the self-governing bodies of the medical profession and other actors in the health sector at the federal and state levels.

Verband der privaten Krankenversicherung e. V. (PKV – Association of Private Health Insurers)

The Association of Private Health Insurers represents and promotes the general interests of private health insur-

ance and its member companies.

The association further serves to voice the position of the private health insurance sector in sociopolitical decisions by issuing position statements and participating in hearings held in the course of national and European legislative processes. The association also supports member companies in resolving fundamental issues relating to structuring premiums.

Verband Forschender Arzneimittelhersteller e. V. (VFA – Association of Research-Based Pharmaceutical Companies)

The Association of Research-Based Pharmaceutical Companies is a trade organisation of research-based pharmaceutical manufacturers in Germany. It represents the interests of globally leading, research-based pharmaceutical manufacturers in health, research and economic policy, particularly by:

- Strengthening Germany as a location for the pharmaceutical industry,
- Eliminating bureaucratic regulation and creating new freedom for self-responsible action,
- Safeguarding dependable, future-oriented framework conditions for the research, development and production of innovative pharmaceuticals in Germany.

Verbund für Angewandte Hygiene (VAH – Association for Applied Hygiene)

The Association for Applied Hygiene promotes the application-oriented, scientific study and implementation of hygiene and hygiene-related issues. This includes the elaboration of test protocols and evaluation standards for decontamination, disinfection, antisepsis and sterilisation procedures; the exchange of ideas and multidisciplinary cooperation with relevant medical and non-medical disciplines; national and international harmonisation of efforts with regard to the indication, toxicological and ecological aspects of products and procedures employed for preventing infections. In addition, the VAH takes a special interest in planning and organising specialist training and continuing education programmes in the area of applied hygiene.

The members of the VAH include scientific societies and professional associations, as well as experts from the fields of hygiene, public health and infectiology.

Vereinigung der Hygiene-Fachkräfte der Bundesrepublik Deutschland e. V. (VHD – Association of Hygiene Professionals in the Federal Republic of Germany)

The Association of Hygiene Professionals in the Federal

Republic of Germany works to provide practical and scientific specialist training for its members and other target groups of the hygiene sector, in an effort to improve hospital hygiene. The association also represents the interests of hygiene professionals at the national and international level. Currently, however, it focuses primarily on national issues.

Vereinigung für Allgemeine und Angewandte Mikrobiologie (VAAM – Association for General and Applied Microbiology)

The Association for General and Applied Microbiology is Germany's largest scientific society in the field of microbiology. The VAAM primarily unites microbiologists focusing on the natural sciences. The Microbial Pathogenicity specialist group also addresses the problem of antimicrobial resistance and pathogenicity research on bacteria.

World Health Assembly (WHA)

The World Health Assembly is the forum that directs the World Health Organization, representing 192 Member States. It convenes once a year and is the world's largest governing body committed to health policy issues. The main tasks of the WHA are to approve the WHO programme and budget for the subsequent two-year period and to make decisions on major policy issues.

World Health Organization (WHO)

The World Health Organization is an international authority within the UN, founded in Geneva in 1948. It addresses health policy issues that go beyond the sphere of national health organisations with the aim of “achieving the best possible state of health for all people”. The WHO's mission is to lead and coordinate global health concerns, support the governments of the Member States in their efforts to expand their public health and healthcare services, control and eradicate global epidemics, promote medical training and scientific research in the fields of medicine, hygiene and public health, and establish international norms and standards, e.g. for drugs and health statistics.

World Organisation for Animal Health (OIE)

The World Organisation for Animal Health is an international authority committed to improving animal health worldwide.

OIE is responsible for the following tasks, among others: n Transparency: each Member State undertakes to report animal diseases it detects in its territory to OIE, which disseminates the information to other countries, which can

then take the necessary preventive action.

- Collecting scientific information: OIE collects all available publications on animal disease and its control, and makes this information available to the Member States.
- International cooperation: OIE promotes an international scientific exchange.
- Establishing standards: OIE elaborates guidelines for controlling animal disease and norms for maintaining hygienic conditions in keeping animals.
- Development aid: OIE supports developing countries with measures to prevent the outbreak of animal diseases.
- Food safety: in the view of OIE, controlling animal disease by optimising the conditions under which animals are kept helps contribute to improving the quality of food of animal origin.

Scientific Institute of the Local Health Care Funds (WIdO)

The Scientific Institute of the Local Health Care Funds is a research organisation that addresses fundamental aspects and problems of statutory health insurance and related fields. Its research activities are designed for practical benefit. They serve the purpose of supporting the health insurance funds in ensuring high-quality and economically efficient healthcare for the public. In this sense, WIdO considers itself to be a link between science and practice. WIdO has all the insurance benefit data (personalised under pseudonyms) for all 24 million insureds of the local health insurance funds, for example from the benefit classes hospital, drugs, outpatient services (e.g. physicians' diagnoses), remedies or sick leave certificates. WIdO furthermore has access to benefit data (anonymous), e.g. in the drug sector, for all the roughly 70 million SHI insureds since 1980. These data form the basis of a number of cooperations with various research institutions, the results of which are published – annually in most cases – in documents such as the Hospital Report, Drug Prescription Report, Absenteeism Report and Remedies Report.

Scientific Commissions of the Robert Koch Institute

The Commission for Infectious Disease, the Commission on Hospital Hygiene and Infectious Disease Prevention (KRINKO) and the Standing Committee on Vaccination (STIKO) are scientific bodies within the Robert Koch Institute.

The Commission for Infectious Disease aims in particular to support the RKI in controlling infectious diseases and to advise it in developing medium and long-term goals (infectious disease research, prevention and control of communicable diseases).

STIKO is anchored in law in Section 20 Para. 2 IfSG. It issues recommendations regarding vaccination practices and other measures relating to the specific prevention of communicable diseases in humans. Further, STIKO develops criteria for distinguishing between a normal reaction to a vaccination and damage to health that exceeds the usual extent of a reaction to a vaccination.

KRINKO is anchored in law in Section 23 Para. 2 IfSG. It is commissioned to draw up recommendations for the prevention of nosocomial infections and for organisational, architectural and functional measures for hygiene in hospitals and other medical facilities.

Within the framework of the consultation phase, the following additional potential players were also identified, with whom cooperation is in the planning to promote implementation of the present strategy:

- Ärztliches Zentrum für Qualität in der Medizin (AZQ – Agency for Quality in Medicine)
- Berufsverband Deutscher Internisten (BDI – German Association of Internists)
- Deutsche Gesellschaft für Allgemeinmedizin und Familienmedizin (DEGAM – German Society for General and Family Medicine)
- Deutsche Gesellschaft für Chirurgie (DGCH – German Society for Surgery)
- Deutsche Gesellschaft für Innere Medizin (DGIM – German Society for Internal Medicine)
- Deutsche Gesellschaft für Unfallchirurgie (DGU – German Society for Trauma and Emergency Surgery)
- Fachgesellschaft für Pädiatrische Infektiologie (DGPI – Society for Paediatric Infectious Diseases)
- Verband der Diagnostica-Industrie (VDGH – Diagnostics Industry Association)

References

1. **Alexy, R.** 2003. Antibiotika in der aquatischen Umwelt: Eintrag, Elimination und Wirkung auf Bakterien. Fakultät für Chemie, Pharmazie und Geowissenschaften der Albert-Ludwigs-Universität Freiburg. Dissertation
2. **Arnold, S. R. and S. E. Straus.** 2005. Interventions to improve antibiotic prescribing practices in ambulatory care. *Cochrane.Database.Syst.Rev.*CD003539.
3. **Beschluss der 79. Gesundheitministerkonferenz der Länder.** 2006. Methicillin-resistente Staphylococcus-aureus (MRSA), TOP 10.1. 30-6-2006. Dessau.
4. **Beyaert, G.** 2002. Das Antibiogramm – Teil 1. *URO-News*16–23.
5. **Beyaert, G.** 2002. Das Antibiogramm – Teil 2. *URO-News*24–28.
6. **Bitter-Suermann, D., R. Marre, U. Ullmann, and B. Wiedemann.** 1998. GENARS (German Network on Antimicrobial Resistance Surveillance): Frühwarnsystem "Mikrobielle Resistenz" – Projekt der Deutschen Gesellschaft für Hygiene und Mikrobiologie und der Paul-Ehrlich-Gesellschaft für Chemotherapie. *Chemotherapie Journal* 7:155–156.
7. **Broll, S., M. Kietzmann, U. Bettin, and L. Kreienbrock.** 2004. Zum Einsatz von Aminoglykosiden, Colistin und β -Laktam-Antibiotika in Fütterungsarzneimitteln für Schweine in Schleswig-Holstein. *Berliner und Münchener Tierärztliche Wochenschrift* 117:398–403.
8. **Broll, S., M. Kietzmann, U. Bettin, and L. Kreienbrock.** 2004. Zum Einsatz von Makroliden, Lincomycin und Tiamulin in Fütterungsarzneimitteln für Schweine in Schleswig-Holstein. *Berliner und Münchener Tierärztliche Wochenschrift* 117:387–391.
9. **Broll, S., M. Kietzmann, U. Bettin, and L. Kreienbrock.** 2004. Zum Einsatz von Sulfonamiden und Sulfonamid/Trimethoprim-Kombinationen in Fütterungsarzneimitteln für Schweine in Schleswig-Holstein. *Berliner und Münchener Tierärztliche Wochenschrift* 117:392–397.
10. **Broll, S., M. Kietzmann, U. Bettin, and L. Kreienbrock.** 2004. Zum Einsatz von Tetrazyklinen in Fütterungsarzneimitteln in der Schweinehaltung in Schleswig-Holstein. *Tierärztliche Praxis* 32:140–145.
11. **Broll, S., M. Kietzmann, U. Bettin, and L. Kreienbrock.** 2002. Zum Einsatz von Fütterungsarzneimitteln in der Tierhaltung in Schleswig-Holstein. *Tierärztliche Praxis* 30:357–361.
12. **Bronzwaer, S., A. Lonroth, and R. Haigh.** 2004. The European Community strategy against antimicrobial resistance. *Euro.Surveill* 9:30–34.
13. **Bundesärztekammer.** 1992. Richtlinien der Bundesärztekammer zur Qualitätssicherung in der Mikrobiologie (Teil A und B). Sonderdruck Deutsches Ärzteblatt 89.
14. **Bundesärztekammer.** 2003. Richtlinie der Bundesärztekammer zur Qualitätssicherung quantitativer laboratoriumsmedizinischer Untersuchungen. *Deutsches Ärzteblatt* 100:A 3335-A 3338.
15. **Bundesärztekammer.** 2004. Kommentar zur "Richtlinie der Bundesärztekammer zur Qualitätssicherung quantitativer laboratoriumsmedizinischer Untersuchungen". Kommentar zur "Richtlinie der Bundesärztekammer zur Qualitätssicherung quantitativer labormedizinischer Untersuchungen".
16. **Bundesärztekammer.** 2007. Empfehlungen zur ärztlichen Fortbildung – Texte und Materialien der Bundesärztekammer zur Fortbildung und Weiterbildung. Empfehlungen zur ärztlichen Fortbildung – Texte und Materialien der Bundesärztekammer zur Fortbildung und Weiterbildung 3.
17. **Bundesärztekammer.** 2007. Musterfortbildungssatzung.
18. **Bundesinstitut für Arzneimittel und Medizinprodukte.** 2006. Resistenzsituation bei systemisch wirkenden Antibiotika: Angaben in den Fachinformationen nun anwenderfreundlich und einheitlich. 17-11-2006.
19. **Bundesministerium für Bildung und Forschung.** 2005. Erläuterungen zur BMBF-Bekanntmachung "Förderung Klinischer Forschergruppen in der Klinischen Infektiologie" vom 05.08.2005.

20. **Bundesministerium für Gesundheit.** 2002. Approbationsordnung für Ärzte. Bundesgesetzblatt Teil 1 Nr. 44, 2405–2435.
21. **Bundesverband für Tiergesundheit.** 2008.
22. **BVL, PEG, IF Freiburg.** GERMAP 2008. Bericht über den Antibiotikaverbrauch und die Verbreitung von Antibiotikaresistenzen in der Human- und Veterinärmedizin in Deutschland.
23. **Carbon, C., O. Cars, and K. Christiansen.** 2002. Moving from recommendation to implementation and audit: part 1. Current recommendations and programs: a critical commentary. *Clin. Microbiol. Infect.* 8 Suppl 2:92–106.
24. **Christ-Crain, M., D. Jaccard-Stolz, R. Bingisser, M. M. Gencay, P. R. Huber, M. Tamm, and B. Müller.** 2004. Effect of procalcitonin-guided treatment on antibiotic use and outcome in lower respiratory tract infections: cluster-randomised, single-blinded intervention trial. *Lancet* 363:600–607.
25. **Christiansen, K., C. Carbon, and O. Cars.** 2002. Moving from recommendation to implementation and audit: part 2. Review of interventions and audit. *Clin. Microbiol. Infect.* 8 Suppl 2:107–128.
26. **Clinical and Laboratory Standards Institute.** 2008. Performance Standards for Antimicrobial Disk and Dilution Susceptibility Tests for Bacteria Isolated from Animals, M31-A3 Vol. 28 No. 8 Replaces M31-A2 Vol. 22 No.6.
27. **Commission of the European Communities.** 2001. Proposal for a Council Recommendation on the prudent use of antimicrobial agents in human medicine. 52001PC0333.
28. **Commission of the European Communities.** 2005. Commission staff working document – Detailed analysis of Member States' reports on the implementation of the Council recommendation (2002/77/EC) on the prudent use of antimicrobial agents in human medicine [COM(2005)684 final].
29. **Committee for Medicinal Products for Veterinary Use and International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products.** 2001. Guidance on pre-approval information for registration of new veterinary medicinal products for food producing animals with respect to antimicrobial resistance. CVMP/VICH/644/01-FINAL.
30. **Cornaglia, G., W. Hryniewicz, V. Jarlier, G. Kahlmeter, H. Mittermayer, L. Stratchounski, and F. Baquero.** 2004. European recommendations for antimicrobial resistance surveillance. *Clin. Microbiol. Infect.* 10:349-383.
31. **Daniels-Hardt, I., F. Verhoeven, A. Mellmann, M. G. Hendrix, J. E. Gemert-Pijnen, and A. W. Friedrich.** 2006. EUREGIO-projekt MRSA-net Twente/Munsterland. Creation of a regional network to combat MRSA. *Gesundheitswesen* 68:674–678.
32. **Davey, P., E. Brown, L. Fenelon, R. Finch, I. Gould, G. Hartman, A. Holmes, C. Ramsay, E. Taylor, M. Wilcox, and P. Wiffen.** 2005. Interventions to improve antibiotic prescribing practices for hospital inpatients. *Cochrane. Database. Syst. Rev.* CD003543.
33. **de Kraker M. and N. van de Sande-Bruinsma.** 2007. Trends in antimicrobial resistance in Europe: update of EARSS results. *Euro.Surveill* 12:E070315.
34. **de Warren A.** Background to programme "Antibiotics are not automatic". Focal Point Meeting at ECDC. 6-12-2007
35. **de With K., M. Steib-Bauert, P. Straach, and W. V. Kern.** 2006. Is there significant regional variation in hospital antibiotic consumption in Germany? *Infection* 34:274–277.
36. **de With, K., H. Schröder, E. Meyer, K. Nink, S. Hoffmann, M. Steib-Bauert, R. Kämmerer, S. Rueß, F. Daschner, and W. Kern.** 2004. Antibiotikaaanwendung in Deutschland im europäischen Vergleich – Antibiotic use in Germany and Europe. *Deutsche Medizinische Wochenschrift* 129:1987–1992.
37. **Deja, M., I. Nachtigall, E. Halle, M. Kastrup, M. Mac Guill, and C. Spies.** 2007. Antibiotikatherapie – Strategien für die Verordnung von Antibiotika in der Intensivmedizin. *Anästhesiol Intensivmed Notfallmed Schmerzther* 2:108–114.
38. **EARSS Management Team.** 2006. EARSS Annual

- Report 2005 – On-going surveillance of *S. pneumoniae*, *S. aureus*, *E. coli*, *E. faecalis*, *K. pneumoniae*, *P. aeruginosa*. National Institute for Public Health and the Environment.
39. **ECDC.** 2007. Annual epidemiological report on communicable diseases in Europe.
 40. **ECDC Advisory Forum.** 2005. Framework for an ECDC Project on Antimicrobial Resistance (AMR). Framework for an ECDC Project on Antimicrobial Resistance (AMR) AF4/10/10:1–6.
 41. **ECDC Advisory Forum.** 2006. Proposed instrument for assessment of member states' actions in combating antimicrobial resistance AF5/12/11:1–14.
 42. **Europäische Kommission.** 2006. Verordnung (EG) Nr. 1177/2006 der Kommission vom 1. August 2006 zur Durchführung der Verordnung (EG) Nr. 2160/2003 des Europäischen Parlaments und des Rates hinsichtlich der Bestimmung über die Anwendung von spezifischen Bekämpfungsmethoden im Rahmen der nationalen Programme zur Bekämpfung von Salmonellen bei Geflügel.
 43. **Europäische Kommission.** 2007. Entscheidung der Kommission vom 12. Juni 2007 zu einer harmonisierten Überwachung von Antibiotikaresistenz von Salmonellen bei Geflügel und Schweinen (Entscheidung 2007/407/EG).
 44. **Europäische Kommission.** 2007. Entscheidung der Kommission vom 19. Juli 2007 über eine Finanzhilfe der Gemeinschaft für eine Erhebung in den Mitgliedstaaten über die Prävalenz und die Resistenz gegen antimikrobielle Mittel von *Campylobacter* spp. in Masthähnchenherden und die Prävalenz von *Campylobacter* spp. und *Salmonella* spp. in Schlachtkörpern von Masthähnchen (Entscheidung 2007/516/EG).
 45. **Europäische Kommission.** 2008. Entscheidung der Kommission vom 20. Dezember 2007 über eine Finanzhilfe der Gemeinschaft für eine Erhebung in den Mitgliedstaaten über die Prävalenz von *Salmonella* spp. und Methicillin-resistentem *Staphylococcus aureus* in Zuchtschweinebeständen (Entscheidung 2008/55/EG).
 46. **Europäischer Rat.** 2008. Council Conclusion on Antimicrobial Resistance (AMR).
 47. **Europäisches Parlament.** 2003. Richtlinie 2003/99/EG des Europäischen Parlaments und des Rates vom 17. November 2003 zur Überwachung von Zoonosen und Zoonoseerregern und zur Änderung der Entscheidung 90/424/EWG des Rates sowie zur Aufhebung der Richtlinie 92/117/EWG des Rates.
 48. **Europäisches Parlament.** 2003. Verordnung (EG) Nr. 2160/2003 des Europäischen Parlaments und des Rates vom 17. November 2003 zur Bekämpfung von Salmonellen und bestimmten anderen durch Lebensmittel übertragbaren Zoonoseerregern.
 49. **Europäisches Parlament.** 2004. Verordnung (EG) Nr. 882/2004 des Europäischen Parlaments und des Rates vom 29. April 2004 über amtliche Kontrollen zur Überprüfung der Einhaltung des Lebensmittel- und Futtermittelrechts sowie der Bestimmungen über Tiergesundheit und Tierschutz.
 50. **European Committee on Antimicrobial Susceptibility Testing.** 2006. EUCAST Procedure for Harmonising and Defining Breakpoints. EUCAST Procedure for Harmonising and Defining Breakpoints.
 51. **European Medicines Agency and Committee for Medicinal Products for Veterinary Use.** 2001. Guideline for the demonstration of efficacy for veterinary medicinal products containing antimicrobial substances. EMEA/CVMP/627/01–FINAL.
 52. **European Medicines Agency and Committee for Medicinal Products for Veterinary Use.** 2001. Reflection paper on the use of fluorquinolones in food producing animals – precautions for use in the SPC regarding prudent use guidance. EMEA/CVMP/416168/2006–Final.
 53. **European Medicines Agency, Committee for Medicinal Products for Veterinary Use, and Scientific Advisory Group on Antimicrobials.** 2005. Public statement on the use of (Fluoro)quinolones in food-producing animals in the European Union: Development of resistance and impact on human and animal health. EMEA/CVMP/SAGAM/184651/05.
 54. **European Medicines Agency, Committee for Medicinal Products for Veterinary Use, and Scientific Advisory Group on Antimicrobials.** 2005. Public statement on the use of (Fluoro)quinolones in food-producing animals in the European Union: Development of resistance and impact on human and animal health. EMEA/CVMP/SAGAM/184651/05.

- sory Group on Antimicrobials.** 2006. Reflection paper on the use of 3rd and 4th generation cephalosporines in food-producing animals in the European Union: development of resistance and impact on human health. EMEA/CVMP/ SAGAM/ 81730/2006-CONSULTATION.
55. **European Medicines Agency, Committee for Medicinal Products for Veterinary Use, and Scientific Advisory Group on Antimicrobials.** 2007. Reflection paper on antimicrobial resistance surveillance as post-marketing authorisation commitment. EMEA/CVMP/SAGAM/428938/2007-CONSULTATION.
 56. **Ferech, M., S. Coenen, S. Malhotra-Kumar, K. Dvorkova, E. Hendrickx, C. Suetens, and H. Goossens.** 2006. European Surveillance of Antimicrobial Consumption (ESAC): outpatient antibiotic use in Europe. *J.Antimicrob.Chemother.* 58:401-407.
 57. **Finch, R. and P. A. Hunter.** 2006. Antibiotic resistance action to promote new technologies: report of an EU Intergovernmental Conference held in Birmingham, UK, 12-13 December 2005. *J.Antimicrob. Chemother.* 58 Suppl 1:i3-i22.
 58. **Fischer, T., S. Fischer, M. M. Kochen, and E. Hummers-Pradier.** 2005. Influence of patient symptoms and physical findings on general practitioners' treatment of respiratory tract infections: a direct observation study. *BMC.Fam.Pract.* 6:6.
 59. **Friedrich, A. W., I. Daniels-Haardt, A. K. Sonntag, F. Verhoeven, L. Gemert-Pijnen, A. Mellman, and R. Hendrix.** 2006. EUREGIO MRSA-net Twente/ Münsterland. *West-fälisches Ärzteblatt* 51-52.
 60. **Friedrich, A. W., I. Daniels-Haardt, J. E. W. C. van Gemert-Pijnen, M. G. R. Hendrix, C. von Eiff, F. Kipp, K. K. R. Becker, F. Verhoeven, and A. Mellmann.** 2007. Ein regionales Netzwerk zur Prävention und Kontrolle von Infektionen durch MRSA: EUREGIO MRSA-net Twente/ Münsterland. *Epidemiologisches Bulletin* 307-311.
 61. **Gastmeier, P., C. Brandt, D. Sohr, R. Babikir, D. Mlageni, F. Daschner, and H. Rüden.** 2004. Postoperative Wundinfektionen nach stationären und ambulanten Operationen – Ergebnisse aus dem Krankenhaus-Infektions-Surveillance-System (KISS). *Bundesgesundheitsblatt – Gesundheitsforschung – Gesundheitsschutz* 47:339-344.
 62. **Gastmeier, P., D. Sohr, C. Geffers, M. Behnke, F. Daschner, and H. Rüden.** 2005. Mortality risk factors with nosocomial *Staphylococcus aureus* infections in intensive care units: results from the German Nosocomial Infection Surveillance System (KISS). *Infection* 33:50-55.
 63. **Geffers, C., J. Koch, A. Nassauer, F. Daschner, H. Rüden, and P. Gastmeier.** 2000. Aufbau einer Referenzdatenbank für nosokomiale Infektionen auf Intensivstationen: Erste Ergebnisse des nationalen Krankenhaus-Infektions-Surveillance-Systems (KISS). *Der Anästhesist* 49:732-737.
 64. **Geffers, C., I. Zuschneid, D. Sohr, H. Rüden, and P. Gastmeier.** 2004. Microbiological isolates associated with nosocomial infections in intensive care units: data of 274 intensive care units participating in the German Nosocomial Infections Surveillance System (KISS). *Anesthesiol.Intensivmed Notfallmed Schmerzther* 39:15-19.
 65. **Geissel, W.** 2007. Neue Tests ermöglichen eine gezielte Antibiose – das hilft Arzneimittel zu sparen und beugt Resistenzen vor. *Ärzte Zeitung.*
 66. **Gonzales, R., J. F. Steiner, and M. A. Sande.** 1997. Antibiotic prescribing for adults with colds, upper respiratory tract infections, and bronchitis by ambulatory care physicians. *JAMA* 278:901-904.
 67. **Goossens, H., M. Ferech, S. R. Vander, and M. Elseviers.** 2005. Outpatient antibiotic use in Europe and association with resistance: a cross-national database study. *Lancet* 365:579-587.
 68. **Goossens, H., D. Guillemot, M. Ferech, B. Schlemmer, M. Costers, M. van Breda, L. J. Baker, O. Cars, and P. G. Davey.** 2006. National campaigns to improve antibiotic use. *Eur.J.Clin Pharmacol.* 62:373-379.
 69. **Grundmann, H.** 2007. Surveillance of antibiotic resistance. *Jahrestagung der Deutschen Gesellschaft für Hygiene und Mikrobiologie e. V.*
 70. **Günther, J., W. Kern, K. Nink, H. Schröder, and K. de With.** 2003. Solange sie noch wirken ... Analysen und Kommentare zum Antibiotikaverbrauch in Deutschland.

71. **Herr, C. E., T. H. Heckrodt, F. A. Hofmann, R. Schnettler, and T. F. Eikmann.** 2003. Additional costs for preventing the spread of methicillin-resistant *Staphylococcus aureus* and a strategy for reducing these costs on a surgical ward. *Infect. Control Hosp. Epidemiol.* 24:673–678.
72. **Höck, M. R. I., S. Swidsinski, B. Eberpracher, L. Schuster, R. Küchler, C. Grubel, U. Futh, L. Michalski, B. Seefeld, E. Zill, R. Zuschneid, R. Schiller, K. Vogt, H. Stetzelberg, B. Hammer, B. Wilbrandt, K. Weist, and J. Wagner.** 2004. Bakterielle Erreger von Krankenhausinfektionen mit besonderen Resistenzen und Multiresistenzen, Teil II. Erfassung und Bewertung gem. § 23 Abs. 1 IfSG in einem regionalen Netzwerk. *Bundesgesundheitsblatt – Gesundheitsforschung – Gesundheitsschutz* 47:363–368.
73. **Höffken, G., J. Lorenz, W. Kern, T. Welte, T. Bauer, K. Dalhoff, E. Dietrich, S. Ewig, P. Gastmeier, B. Grabein, E. Halle, M. Kolditz, R. Marre, and H. Sitter.** 2005. S3–Leitlinie zu Epidemiologie, Diagnostik, antimikrobieller Therapie und Management von erwachsenen Patienten mit ambulant erworbenen tiefen Atemwegsinfektionen. Georg Thieme Verlag KG, Stuttgart, New York.
74. **Huppertz, K. and B. Wiedemann.** 2000. GENARS-Projekt etabliert. *Chemotherapie Journal* 9:200–212.
75. **INSTAND.** 2006. Struktur von INSTAND e. V.
76. **Kern, W., K. Aktories, and H. Bertz.** 2006. Leitlinien Antimikrobielle Therapie bei erwachsenen Intensivpatienten und kritisch Kranken. Universitätsklinikum Freiburg – Arzneimittelkommission.
77. **Kern, W. V., K. de With, M. Steib-Bauert, M. Fellhauer, A. Plangger, and W. Probst.** 2005. Antibiotic use in non-university regional acute care general hospitals in southwestern Germany, 2001–2002. *Infection* 33:333–339.
78. **Kist, M., E. Glocker, and S. Suerbaum.** 2005. Pathogenese, Diagnostik und Therapie der *Helicobacter pylori*-Infektion. *Bundesgesundheitsblatt – Gesundheitsforschung – Gesundheitsschutz* 48:669–678.
79. **Kommission für Krankenhaushygiene und Infektionsprävention.** Mitteilung der Kommission für Krankenhaushygiene und Infektionsprävention zur Surveillance (Erfassung und Bewertung) von nosokomialen Infektionen (Umsetzung von § 23 IfSG). 2001. *Bundesgesundheitsblatt – Gesundheitsforschung – Gesundheitsschutz* 44:523–536.
80. **Kompetenznetz Ambulant Erworbene Pneumonie.** 2007. Standorte. 22-5–2007.
81. **Kresken, M.** 2003. Resistente Bakterien in Deutschland – Wie groß sind die Gefahren? *Medizinische Monatsschrift für Pharmazeuten* 26:38–44.
82. **Kresken, M.** Aktuelle Daten zur Resistenzsituation bei Bakterien gegenüber Antibiotika – Ergebnisse der PEG-Resistenzstudie 2004. 29-11–2005.
83. **Kresken, M., D. Hafner, F.-J. Schmitz, and T. Wichelhaus.** 2004. PEG-Resistenzstudie – Resistenzsituation bei klinisch wichtigen Infektionserregern gegenüber Antibiotika in Deutschland und im mitteleuropäischen Raum. Paul-Ehrlich-Gesellschaft für Chemotherapie e. V. and Arbeitsgemeinschaft Empfindlichkeitsprüfungen & Resistenz.
84. **Langner, I. and G. Selke.** 2006. Arzneitherapie: Gut beraten – klug verordnen. *Gesundheit und Gesellschaft* 26–32.
85. **Mannien, J., S. van den Hof, C. Brandt, M. Behnke, J. C. Wille, and P. Gastmeier.** 2007. Comparison of the National Surgical Site Infection surveillance data between The Netherlands and Germany: PREZIES versus KISS. *J. Hosp. Infect.* 66:224–231.
86. **Mauch, H., R. Lütticken, and S. Gatermann.** 1999. Neue Mikrobiologisch-Infektiologische Qualitätsstandards (MIQ) der DGHM (früher Verfahrensrichtlinien). *Chemotherapie Journal* 8.
87. **Meyer, E. and P. Gastmeier.** 2007. Antibiotikatherapie – Einfluss und Methodik der Surveillance. *Anästhesiol Intensivmed Notfallmed Schmerzther:* 116–121.
88. **Meyer, E., D. Jonas, F. Schwab, P. Gastmeier, H. Rüden, and F. D. Daschner.** 2004. SARI: Surveillance der Antibiotikaaanwendung und bakteriellen Resistenzentwicklung auf deutschen Intensivstationen – Zu den Zusammenhängen von Antibiotikaverbrauch

- und Resistenzsituation. Bundesgesundheitsblatt – Gesundheitsforschung – Gesundheitsschutz 47:345–351.
89. **Meyer, E., D. Jonas, F. Schwab, H. Rueden, P. Gastmeier, and F. D. Daschner.** 2003. Design of a surveillance system of antibiotic use and bacterial resistance in German intensive care units (SARI). *Infection* 31:208–215.
 90. **Meyer, E., F. Schwab, P. Gastmeier, D. Jonas, H. Rueden, and F. D. Daschner.** 2006. Methicillin-resistant *Staphylococcus aureus* in German intensive care units during 2000–2003: data from Project SARI (Surveillance of Antimicrobial Use and Antimicrobial Resistance in Intensive Care Units). *Infect Control Hosp.Epidemiol.* 27:146–154.
 91. **Meyer, E., F. Schwab, P. Gastmeier, H. Rueden, and F. D. Daschner.** 2006. Surveillance of antimicrobial use and antimicrobial resistance in German intensive care units (SARI): a summary of the data from 2001 through 2004. *Infection* 34:303–309.
 92. **MRSA-net.** 2006. Informationen zum MRSA-net Projekt – Die Projektziele.
 93. **Müller-Bahrndt, D.** 2004. Entwicklung des Einsatzes antimikrobiell wirksamer Tierarzneimittel in Fütterungsarzneimitteln in Sachsen-Anhalt in den Quartalen 03/2000, 01/2001, 03/2001 und 01/2002 und einer ausgewählten Großtierpraxis im 1.Quartal 2002, 1–138. Institut für Pharmakologie, Pharmazie und Toxikologie der Veterinärmedizinischen Fakultät der Universität Leipzig. Dissertation
 94. **Nink, K., H. Schröder, and I. Schubert.** 2005. Arzneimittel, p. 99–122. In: I. P. Swart E (ed.), *Routinedaten im Gesundheitswesen. Handbuch Sekundärdatenanalyse: Grundlagen, Methoden, Perspektiven.* Verlag Hans Huber, Bern.
 95. **Nink, K. and H. Schröder.** 2003. Antibiotika maßvoll einsetzen. *Gesundheit und Gesellschaft* 6:14–15.
 96. **Noll, I., K. Heckenbach, N. Kleinkauf, and T. Eckmanns.** 2007. Zur Surveillance der Antibiotikaresistenz in Deutschland. *Epidemiologisches Bulletin* 44:405–409.
 97. **Official Journal of the European Communities.** 2002. Council Recommendation of 15 November 2001 on the prudent use of antimicrobial agents in human medicine. L 34/13.
 98. **OIE, World Organisation for Animal Health.** 2006. Guidelines for the harmonisation of national antimicrobial resistance surveillance and monitoring programmes, In: *Terrestrial Animal Health Code.*
 99. **OIE, World Organisation for Animal Health.** 2006. Guidelines for the monitoring of the quantities of antimicrobials used in animal husbandry, In: *Terrestrial Animal Health Code.*
 100. **OIE, World Organisation for Animal Health.** 2006. Guidelines for the responsible and prudent use of antimicrobial agents in veterinary medicine, In: *Terrestrial Animal Health Code.*
 101. **OIE, World Organisation for Animal Health.** 2006. Risk assessment for antimicrobial resistance arising from the use of antimicrobials in animals, In: *Terrestrial Animal Health Code.*
 102. **Oppermann, H., B. Thriene, and S. Zaumseil.** 2005. Bundeslandspezifische Meldepflicht als Ergänzung zur Meldepflicht des IfSG: Landesspezifische Meldepflicht in Sachsen-Anhalt. *Bundesgesundheitsblatt – Gesundheitsforschung – Gesundheitsschutz* 48:990–997.
 103. **Peterson, L. R. and A. Dalhoff.** 2004. Towards targeted prescribing: will the cure for antimicrobial resistance be specific, directed therapy through improved diagnostic testing? *J.Antimicrob. Chemother.* 53:902–905.
 104. **Petursson, P.** 2005. GPs' reasons for “non-pharmacological” prescribing of antibiotics. A phenomenological study. *Scand.J.Prim.Health Care* 23:120–125.
 105. **Robert Koch-Institut.** 2003. Zum Antibiotikaverbrauch und zu bakteriellen Resistenzen auf Intensivstationen – Aktuelle Daten des Projektes SARI – Stand September 2002. *Epidemiologisches Bulletin* 18:140–141.
 106. **Robert Koch-Institut.** 2004. Aktuelle Daten des Krankenhaus-Infektions-Surveillance-Systems (KISS): Surveillance nosokomialer Infektionen in Intensivstationen. *Epidemiologisches Bulletin* 41:349–351.
 107. **Robert Koch-Institut.** 2005. Zur Tätigkeit des

- Nationalen Referenzzentrums (NRZ) für *Helicobacter pylori*. *Epidemiologisches Bulletin* 24:203–210.
108. **Robert Koch-Institut.** 2007. Empfehlungen der Kommission für Krankenhaushygiene und Infektionsprävention (KRINKO). http://www.rki.de/nn_206124/DE/Content/Infekt/Krankenhaushygiene/Kommission/kommission__node.html?__nnn=true.
 109. **Robert Koch-Institut.** 2007. Nationale Referenzzentren und Konsiliarlaboratorien in der aktuellen Berufungsperiode (2005 bis 2007). 1–51.
 110. **Rodloff, A., T. Bauer, S. Ewig, P. Kujath, and E. Müller.** 2008. Sensibel, intermediär und resistent – Wirksamkeit von Antibiotika. *Deutsches Ärzteblatt* 39:657–662.
 111. **Schnitzler, N., Wallmann, J., Mielke, M., and Schwarz, S.** 2006. Antibiotikaverbrauch und -Resistenz – Wo steht Deutschland? Symposium der Initiative GERMAP.
 112. **Schröder, H., K. Nink, J. Günther, and W. Kern.** 2006. Antibiotika: Solange sie noch wirken ... Revisited: 2001-2004. 1–37.
 113. **Schröder, H., K. Nink, J. Günther, and W. V. Kern.** 2003. Antibiotika: Solange sie noch wirken ... Aktuelle Studie zum Antibiotikaeinsatz in Deutschland. *GGW* 3:7–16.
 114. **Schröder, H., K. Nink, and A. Zawinell.** 2004. Transparenz jetzt nutzen – Einführung in die Arzneimittelverbrauchsforschung. *Deutsche Apotheker Zeitung* 144:63–68.
 115. **Schwartz, T., W. Kohnen, B. Jansen, and U. Obst.** 2003. Detection of antibiotic-resistant bacteria and their resistance genes in wastewater, surface water, and drinking water biofilms. *FEMS Microbiology Ecology* 43:325–335.
 116. **Shah, P. M.** 2001. Zum Stellenwert des Agardiffusionstests. *Chemotherapie Journal* 218–220.
 117. **Spies, C. D., I. Nachtigall, M. Kastrup, and M. Deja.** 2007. Antibiotikatherapie – Standards, Richtlinien und Empfehlungen für die Antibiotikatherapie. *Anesthesiol.Intensivmed Notfallmed Schmerzther* 106–107.
 118. **Stock, I., K. Machka, A. Rodloff, and B. Wiedemann.** 2001. Qualitätssicherung und Qualitätskontrollen in der Antibiotika-Empfindlichkeitsbestimmung von Bakterien mit der Mikrodilution. *Chemotherapie Journal* 78–98.
 119. **Surveillance der Antibiotika-Anwendung und der bakteriellen Resistenzen auf Intensivstationen (SARI) – Pilotprojekt.** 2007. 1–16.
 120. **The European Agency for the Evaluation of Medicinal Products.** 2004. Note for Guidance on Evaluation of Medicinal Products Indicated for Treatment of Bacterial Infections (CPMP/EWP/558/95 rev 1).
 121. **Vander Stichele, R. H., M. M. Elseviers, M. Ferech, S. Blot, and H. Goossens.** 2006. Hospital consumption of antibiotics in 15 European countries: results of the ESAC Retrospective Data Collection (1997–2002). *J.Antimicrob.Chemother.* 58:159–167.
 122. **Vogel, F., H. Scholz, B. Al-Nawas, W. Elies, M. Kresken, H. Lode, O. Müller, K. G. Naber, E. Petersen, F. Sörgel, W. Stille, C. Tauchnitz, M. Trautmann, U. Ullmann, H. Wacha, and B. Wiedemann.** 2002. Rationaler Einsatz oraler Antibiotika bei Erwachsenen – Empfehlungen einer Expertenkommission der Paul-Ehrlich-Gesellschaft für Chemotherapie e. V. *Chemotherapie Journal* 11:47–58.
 123. **Vogel, F., H. Worth, D. Adam, J. Lorenz, H. Scholz, W. Stille, K. Unertl, and B. Wiedemann.** 2000. Rationale Therapie bakterieller Atemwegsinfektionen – Empfehlungen einer Expertengruppe der Paul-Ehrlich-Gesellschaft für Chemotherapie e. V. und der Deutschen Atemwegsliga e. V. *Chemotherapie Journal* 9:3–23.
 124. **Wernitz, M. H., S. Keck, S. Swidsinski, S. Schulz, and S. K. Veit.** 2005. Cost analysis of a hospital-wide selective screening programme for methicillin-resistant *Staphylococcus aureus* (MRSA) carriers in the context of diagnosis related groups (DRG) payment. *Clin.Microbiol.Infect.* 11:466–471.
 125. **Wernitz, M. H., S. Swidsinski, K. Weist, D. Sohr, W. Witte, K. P. Franke, D. Roloff, H. Ruden, and S. K. Veit.** 2005. Effectiveness of a hospital-wide selective screening programme for methicillin-resistant *Staphylococcus aureus* (MRSA) carriers at hospital

- admission to prevent hospital-acquired MRSA infections. *Clin.Microbiol.Infect.* 11:457–465.
126. **Witte, W., M. Mielke, A. Ammon, A. Nassauer, and N. Wischnewski.** 2005. Fachtagung der AG Nosokomiale Infektionen am RKI zur Intensivierung der Umsetzung von Präventionsstrategien bei MRSA. *Epidemiologisches Bulletin* 31–38.
127. **Witte, W., M. Mielke, A. Ammon, A. Nassauer, and N. Wischnewski.** 2006. Fachtagung der AG Nosokomiale Infektionen am RKI zur Intensivierung der Umsetzung von Präventionsstrategien bei MRSA. *Chemotherapie Journal* 1–7.
128. **World Health Organization.** 2001. WHO Global Strategy for Containment of Antimicrobial Resistance. WHO/CDS/CSR/DRS/2001.2.

About this publication

Publisher:

Federal Ministry of Health
Public Relations Division
D-11055 Berlin
Germany

Design: Schleuse01 Werbeagentur GmbH

Printing: Bonifatius, Paderborn

Photos: F1Online, Getty Images, iStockphoto, matton images

Printed on recycled paper

Status: November 2008

If you want to order this brochure:

Order No.: BMG-P-07067
E-mail: publikationen@bundesregierung.de
Telephone: +49 (0)1805 778090*
Fax: +49 (0)1805 778094*
By post: Publikationsversand der Bundesregierung
Postfach 48 10 09
D-18132 Rostock, Germany

* Each call costs 14 cents per minute from German landlines;
different rates may apply to calls from mobile phones.

Information offers of the Federal Ministry of Health

Citizens' Hotline

The Citizens' Hotline of the Federal Ministry of Health is available Mondays to Thursdays from 8.00 a.m. to 6.00 p.m., and Fridays from 8.00 a.m. to 12.00 noon, on the following telephone numbers (calls are charged):

Questions on insurance cover

+49 (0)1805 9966-01*

Questions on health insurance

+49 (0)1805 9966-02*

Questions on long-term care insurance

+49 (0)1805 9966-03*

Questions on health prevention

+49 (0)1805 9966-09*

Questions on drug prevention

+49 (0)221 892031**

Service for the deaf/hard-of-hearing, textphone

+49 (0)1805 9966-07*

Sign-language telephone, ISDN videophone

+49 (0)1805 9966-06*

Sign-language telephone, Video over IP

gebaerdentelefon.bmg@sip.bmg.buergerservice.bund.de

Newsletter

If you would like to receive fortnightly information on the subjects of health, long-term care and health prevention, subscribe to our Newsletter at: www.bmg-newsletter.de

Health Policy Information

The Health Policy Information series is published every two months and deals with topics from the fields of health, long-term care and prevention. The free publication is sent to you by post. Subscribe at: www.bmg-gpi.de

List of publications

You can request the latest list of publications by the Federal Ministry of Health free of charge at any time:

Order No.: BMG-G-07014

E-mail: publikationen@bundesregierung.de

Tel.: +49 (0)1805 778090*

Fax: +49 (0)1805 778094*

Post: Publikationsversand der Bundesregierung

Postfach 48 10 09

D-18132 Rostock, Germany

Internet portal

The latest information from the Federal Ministry of Health can be found at: www.bmg.bund.de

* Each call costs 14 cents per minute from German landlines; different rates may apply to calls from mobile phones.

** BZgA information telephone on drug prevention:
Mon–Thu 10.00 a.m. to 10.00 p.m., Fri–Sun 10.00 a.m. to 6.00 p.m.

This brochure is published as part of the public relations work of the Federal Ministry of Health. It may not be used by political parties, candidates or election workers for canvassing during an election campaign. This applies to European Parliament, Bundestag, Landtag and municipal elections. In particular, abuse is constituted by distribution at election events or on the information stands of political parties, and the insertion, imprinting or affixing of party political information or advertising material. Similarly forbidden is distribution to third parties for the purpose of election campaigning. Regardless of when, how and in what quantities this publication was received by the recipient, it may not be used – even in no connection with the time frame of an impending election – in any manner which could be interpreted as partiality of the Federal Government towards individual political groups.