Priority Medicines

Antimicrobial Resistance

Research Programme
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2 Samenvatting

Antimicrobiële resistentie (AMR) is meer en meer een gevestigd probleem. Een probleem waar de gezondheidszorg al langere tijd tegen streed, en waar nu ook de algemene bevolking mee te maken krijgt. Nederland is redelijk succesvol in de bestrijding van sommige (determinanten van) AMR, zoals bijvoorbeeld in de bestrijding van methicilline resistent S.aureus (MRSA) die vanuit buitenlandse ziekenhuizen de Nederlandse ziekenhuizen binnenkomt. Maar meer algemeen is AMR een probleem wat in een internationale context moet worden gezien. Toegenomen migratie en internationaal reizigersverkeer faciliteren de verspreiding van resistente micro-organismen. Migranten en reizigers brengen antimicrobiële middelen mee die ze in andere landen gekocht hebben, en ook de verkoop van die middelen via het internet is moeilijk te controleren. De aanwezigheid van AMR organismen bij dieren, in voedsel en in het leefmilieu kan niet los worden gezien van AMR bij de mens, en hier ligt misschien wel de grootste uitdaging. Het therapeutisch gebruik van antimicrobiële middelen in de veehouderij is de afgelopen tien jaar verdubbeld in Nederland. AMR stijgt parallel aan de stijging van het gebruik van antimicrobiële middelen bij vee. MRSA bij varkens, en extended spectrum beta-lactamase (ESBL) producerende organismen bij pluimvee, worden momenteel als een groot probleem voor de volksgezondheid gezien.

Om AMR te bestrijden, en om nieuwe antimicrobiologische medicijnen te helpen ontwikkelen, start ZonMw het onderzoeksprogramma Priority Medicines Antimicrobial Resistance. Dit onderzoeksprogramma zal met 14,8 miljoen euro fundamenteel en toegepast onderzoek binnen vijf onderzoeksthema´s ondersteunen:

1. Antibioticagebruik en het ontstaan van resistentie en transmissie
2. Mechanismen en targets voor nieuwe geneesmiddelen
3. Nieuwe technologische ontwikkelingen, met name sneldiagnostiek
4. Optimalisering van antibioticatherapie: dosering en gebruik
5. Innovatieve benaderingen om resistentie te voorkomen

Deze thema´s zijn in overeenstemming met de aanbevelingen van de Wereldgezondheidsorganisatie, die oproepen om onderzoek te verrichten naar: (a) nieuwe manieren om infectieziekten te voorkomen en te bestrijden (thema´s 2, 4 en 5); (b) nieuwe, snelle diagnostiek (thema 3); en (c) surveillance te optimaliseren (thema 1). Onderzoek naar nieuwe aangrijtingspunten voor medicijnen of vaccins vormt een onderdeel van het onderzoeksprogramma. De daadwerkelijke ontwikkeling van medicijnen of vaccins heeft geen plaats binnen dit programma. Voor alle onderzoeksthema´s wordt modellering - als onderzoeksmethode – van grote waarde geacht. Modellering kan, als systematische en disciplineoverstijgende techniek, kennislacunes aan het licht brengen en beleidsbeslissingen ondersteunen.
3 Introduction

In 2004 the World Health Organisation (WHO) signalled the emergence of antimicrobial resistance (AMR), along with a steady decline in the discovery of new antimicrobials. The WHO highlighted four control strategies to help stem the tide: (a) surveillance; (b) prevention; (c) research and product development; and (d) international cooperation (1). Today, AMR can no longer be qualified as merely emerging: it has become an established reality in health care and has begun to spread in nursing homes and the community. In the Netherlands, methicillin resistant \textit{S. aureus} (MRSA) was found in 0.1\% of healthy individuals and in 6\% of nursing home residents. Ciprofloxacin resistant \textit{S. aureus} was found in healthy individuals (0.8\%), patients in general practices (0.3\%) and in nursing home residents (28\%). In healthy carriers – children and adults – \textit{S. pneumoniae} was resistant to clarithromycin (9 and 16\%), co-trimoxazole (5 and 9\%) and doxycycline (11 and 18\%) (2).

The Netherlands has worked hard to keep AMR at bay – and has been successful in doing so in some areas, e.g. with its search-and-destroy policies to keep foreign MRSA out of its hospitals. However, AMR in general cannot be stopped at national borders. International travel and migration facilitates the spread of organisms, resistant or not. Extensively drug resistant tuberculosis is probably the most dreaded example of the havoc caused by a suboptimal use of antimicrobials and migration and travel. Drug taking habits spread as well as microbes do. The relative sparse use of antimicrobials in the Dutch population is challenged by over the counter sales in other countries (brought in by migrants and travellers) as well as by drug sales through the internet.

The presence of resistant organisms in food, animals and the environment is intertwined with human health, and here lies another important challenge for the Netherlands. Therapeutic usage of antimicrobials in animal husbandry has almost doubled in the past decade in The Netherlands. Resistance levels in animal organisms show an increase in parallel with the increase in antimicrobials, both for individual drugs and multi-drug resistance (MDR) (3). MDR non-pathogens can hold their ground in an environment where antimicrobial use is ubiquitous. The Dutch Ministry of Agriculture, Nature and Food Quality (LNV) has sealed a pact between animal husbandry organisations in various production sectors (pigs, poultry, veal calves, cattle) to reduce AMR. A transparent and rational use of antimicrobials, enhanced monitoring of the use of antimicrobials and research are all part of this pact.

There are three ways of transmission of animal AMR to humans. First, the transmission of resistant pathogens, \textit{Salmonella} spp. and \textit{Campylobacter} spp. in particular, can occur through egg and meat consumption (4-6). Second, through direct or indirect (e.g. inhalation) contact resistant animal organisms can infect or populate humans. This is the case with MRSA (non-typeable MRSA or NT-MRSA) from pigs, which is transmitted mainly through skin contact (7). Or, third, resistance genes are transmitted to human pathogens, as vancomycin resistant \textit{enteroccus} species do (3-5). MRSA from pigs and extended spectrum beta-lactamase (ESBL) producing organisms in poultry are, in particular, considered a threat to human health at present.
In recent times some microbes have surprised scientists and policy makers alike. Not behaving in a predictable way – i.e.: resistance is caused by exposure to antimicrobials – these microbes showed that resistance can originate and persist in an erratic fashion. The clearest example is the H1N1 influenza that circulated last winter. The resistance rates ranged from 3 – 97% between different countries, with no apparent relationship to the overuse of antiviral drugs. Another example is community-acquired MRSA (ca-MRSA); again, there is no clear relationship to the over usage of antimicrobials but still it has grown to be a bigger public health problem than the so feared vancomycin resistant S. aureus (8).

This makes surveillance and international collaboration all the more important. Much work has been done in Europe since the WHO signalled a rise in AMR in combination with a decline of new antimicrobials. For example, the establishment of the European Centre for Disease Prevention and Control (ECDC) provided a major opportunity for an enhanced EU-wide surveillance system. The Dutch National Institute for Public Health and the Environment (RIVM) has played an important part herein and continues to do so.

The ECDC acknowledges AMR as one of the major threats related to infectious disease, together with health care related infections, HIV, tuberculosis, influenza and pneumococcal infections (9). However, product development of new antimicrobials has lagged behind surveillance and international collaboration.

To help control AMR and to foster the development of new antimicrobials the Netherlands organisation for health research and development (ZonMw) opens up the research programme Priority Medicines Antimicrobial Resistance. With 14.8 million Euros ZonMw will fund basic and applied research over a period of nine years. The programme’s focus is on antibacterial resistance, but research that concerns AMR in viruses or fungi is also considered for funding, to a limited extent.

In a programming study (2007) five research areas were identified:

1. The role of antimicrobial use in inducing and transmitting resistance
2. Mechanisms and targets for new drugs
3. New technologies, in particular rapid diagnostics
4. Optimising antimicrobial therapy: dosage and use
5. Innovative approaches in antimicrobial resistance prevention

These areas are in accordance with WHO’s recommendations to conduct fundamental and applied research in to (a) novel approaches in optimising prevention and control of infectious disease (areas 2, 4 and 5); (b) new, rapid diagnostics (area 3); and (c) optimising surveillance (area 1) (1). The development of new drugs or vaccines has no place in the programme though the discovery of new points of action for drugs or vaccines, is clearly a part of this research programme. For all research areas the methodology of infectious disease modelling is considered of particular value. As a systematic and overarching approach to the control of infectious disease, it can help identify knowledge gaps and facilitate policy decision making. The Dutch Ministry of Health (VWS) commissioned ZonMw to open the programme Priority Medicines Antimicrobial Resistance (Appendix
12.1). VWS stressed the link between human and animal AMR, and emphasized the importance of the collaboration with LNV in the preparation of the research programme and beyond.

This document describes the Priority Medicines Antimicrobial Resistance research programme. It builds on information from the programming study and technical input from consulted experts (Appendix 12.2). First, the logical framework of the programme is outlined (Section 4). The general and specific objectives of the programme are laid down here, jointly with its’ expected results and verifiable indicators (Appendix 12.3). Section 5 describes the five research areas within the programme, and gives examples of relevant research questions. Links to other initiatives are summarised in Section 6. Organisational aspects of the programme form the last part of this document, with Communication and implementation (Section 7); Organisation of the programme (Section 8); Monitoring and evaluation (Section 9) and finally Funding structure (Section 10).
4 Logical framework

The general aim of the programme is to contribute to the control of antimicrobial resistance, by stimulating research in the field of antibiotics’ use and the development of new medicines or interventions.

Specific goals
- To further our understanding of the role of antimicrobial use in inducing and transmitting resistance
- To help identify mechanisms and targets for new antimicrobial drugs or vaccines
- To facilitate the development of new techniques in the control of antimicrobial resistance
- To contribute to optimising antimicrobial therapy both in dosage and in use
- To stimulate innovative preventive measures to be used in infectious disease control
- To stimulate a systematic and overarching approach in AMR control

The specific goals are related to the five research themes, but also include: (a) to stimulate knowledge transfer and to create the conditions necessary to implement research results; (b) to foster collaboration between:
- research, policy and practice
- animal and human health
- public and private partners

In addition, to foster international collaboration, especially with countries with extensive AMR, such as Eastern and Southern European countries. Appendix 12.3 gives a detailed overview of the programme’s objectives, expected results and verifiable indicators.
5 Research areas

This section describes the five research areas within the programme, and gives examples of relevant research questions. **Mathematical modelling** is considered a useful research method in all research areas. It can build bridges between the domains of research, policy and practice, and between individual and population level research. Expertise in infectious disease modelling is present at different research groups in the Netherlands. A joint project on the spatiotemporal dispersal of MRSA in the Netherlands is running at present (4).

5.1 The role of antimicrobial use in inducing and transmitting resistance

This research area focuses on the epidemiology of AMR, and the role of antimicrobial use in the introduction, spread and transmission of AMR. For this area links to (international) surveillance systems are relevant. In the Netherlands both human and animal AMR is surveyed systematically, as is antimicrobial use (4;10).

Human data are reported annually in NethMap. SWAB, the RIVM, NIVEL, regional Institutes for Public Health Services (GGDs) and the Academic Hospital of Maastricht play an important role in collecting and reporting the data. Its main parts are:

a) The surveillance of AMR in the primary care population, e.g. patients of primary care physicians
b) The surveillance of AMR in secondary and tertiary care populations
c) The surveillance of AMR in hospital isolates
d) The surveillance of AMR in *M.tuberculosis*, *N.gonorrhoea* and *H.pylori* isolates

And:
e) The epidemiology of MRSA in the Netherlands (2).

Veterinary data are surveyed by VANTURES and reported annually in MARAN. Participating organisations in VANTURES are the CVI, the Animal Health Service Deventer, VWA, RIVM and the University of Utrecht. SWAB and VANTURES report to ABRES, an interdepartmental platform of VWS and LNV (10). Data from NethMap and MARAN, used in our introduction, illustrate the extent of AMR in the Netherlands. Quite some research has stemmed from NethMap and MARAN information: MRSA in pigs and ESBL producing organisms in poultry are the focus of current research. Moreover, it has induced present research into AMR in farm animals. The role of companion animals - such as horses, cats and dogs – as a reservoir is not clear. However, isolated findings of resistant isolates have been recorded (5;11).

Other ecosystems, e.g. water, soil and plants, possibly play a role in AMR of human microorganisms. The environment may be contaminated by antimicrobials from human and animal medicine, and from plant production. These antimicrobials, presumably present in sub-lethal concentrations, might then induce selection for resistant organisms. Or: resistance genes can accumulate, in soil for example, and subsequently transfer to organisms living on other species (12). In conclusion, it is undisputed that
human microorganisms are influenced by antimicrobials and resistant organisms or genes that are present in food, animals and the environment. But how the flow of resistant organisms between these different reservoirs goes on, and what the main determinants of spread are, remains largely unknown.

Apart from antimicrobials, biocides may contribute to the increase of AMR. Biocides are disinfectants, antiseptics, preservatives and sterilants used in health care, food production and in consumer products such as tooth paste or cleaning fluids. Some resistance mechanisms are common to both biocides and antimicrobials. Scientific evidence indicates that the use of active molecules in biocidal products may contribute to the increased occurrence of AMR. However, the exact risk of the use of biocides is not clear at present (13).

Relevant research questions in this area include:

- What are the main routes of AMR transmission? Between animals and humans? Between other ecosystems and humans? What is the contribution of biocides?
- Which are the most important risk factors that influence these transmission routes?
- How can the quality and effectiveness of AMR surveillance be improved?
- What is the relative contribution of horizontal gene transfer and mutation followed by clonal transmission to observed epidemiological trends?
- To what extent do bacterial ecologies of resistant organisms in the Netherlands differ from those in other countries?
- What is the role of the genetic and immunological make-up of the host population in shaping the evolution of successful AMR clones?
- Does AMR diminish or disappear after the discontinuation of antimicrobials? If so, how long does it take?

5.2 Mechanisms and targets for new drugs

This research area focuses on the identification of mechanisms and targets for new drugs in relation to microbial evolution. In this context, the uptake of research outcomes by private partners deserves attention. Fundamental, exploring research can provide a building block for new antimicrobials. A rationale approach is necessary: What is it exactly that makes us ill? Can we neutralise this ill-making effect? This research area has direct links to research programmes from TI Pharma and Immunovalley.

Within TI Pharma, industrial and academic research consortia work together in cross-disciplinary research projects that fit into the Priority Medicines program of the WHO. Each year, the Dutch government funds the institute with 30 million Euros. The pharmaceutical industry and academia each contribute an additional 15 million Euros annually. One of the themes in the TI Pharma portfolio is infectious diseases, and within this theme, two AMR research projects are running at present: (1) new antibiotics to fight antimicrobial resistance and (2) protective human antibodies against MRSA.

Immunovalley is a network consortium of 27 partners from knowledge institutes, local and regional governments and private companies. Instituted in 2007 by the Dutch Ministry of Economic Affairs,
Immunovalley aims to connect human and animal health. At present it controls and coordinates ALTANT. This is a research programme of LNV that investigates the alternatives to antimicrobial use in animal husbandry. Recently, four projects have been awarded funding: (a) control of *S. suis* by use of phage therapy and lysins; (b) animal specific immunomodulatory antimicrobials; (c) evasion molecules in staphylococcal bovine mastitis vaccines and (d) identification of immune enhancing phytochemicals that raise resistance to coccidiosis and colibacillosis.

Relevant research questions in this area include:

- Can mechanisms and targets for new drugs be identified?
- What passive or active immune therapies can be used?
- Can alternatives to antimicrobial use be identified?
- What are the underlying mechanisms that determine the evolutionary behaviour of AMR organisms? This includes molecular epidemiology and physiological studies.

### 5.3 New technologies, in particular rapid diagnostics

Improvements in diagnostic tests can streamline diagnosis and treatment of infectious disease. Innovative diagnostic tests are less invasive, give more rapid results and are easier to do (point-of-care tests vs. laboratory tests for example). Rapid diagnostics can improve initial antimicrobial prescription in cases of infection with AMR pathogens and assist physicians in their decision to prescribe or withhold empirical therapy. The main challenge in infectious disease control is to develop point-of-care assays that can rapidly detect multiple pathogens, including their resistance patterns (14).

Multiple techniques for rapid diagnostic testing are expected to become available for clinical use over the coming years. The cost-effectiveness of these tests needs to be carefully determined. The effect of rapid diagnostic testing of MRSA-colonisation on the number of patient-isolation days is currently being evaluated in a multi-centre study in the Netherlands. The achievement of uniformity of testing, also internationally, deserves attention. The focus should be on phenotyping organisms (i.e. determining the characteristics needed for clinical decision making) instead of genotyping them.

Relevant research questions include:

- Can novel approaches for diagnostic testing of AMR microorganisms be developed?
- Can we distinguish between causative organisms quickly, in particular between bacterial and viral infections? Or can a test be developed that indicates the severity of the infection?
- What is the sensitivity and specificity of new diagnostics?
- How cost-effective are new diagnostic tests for AMR microorganisms?
- What are the long-term predictions for the (cost-) effectiveness of patient admission and discharge screening with a view to future public health threats?
- How can new approaches for rapid diagnostic testing best be implemented?
5.4 Optimising antimicrobial therapy

Research in this area contributes to the quality, safety and efficacy of antimicrobial use in different settings. The most favourable antimicrobial therapy has an optimal prescription, dosage (including timing) and use. Optimum dosage and reductions in the length of antimicrobial treatment may alleviate the selection pressure for antimicrobial resistance. Optimum timing is important in the prevention of infections, e.g. in surgery (15). Patients’ and doctors’ behaviour comes in to play when an optimal treatment scheme is described in a guideline or protocol.

A series of interventions is being used to try and influence both doctors’ prescription and patients’ use of antimicrobials. For example, in Belgium, general practitioners get feedback on their own quantitative prescription behaviour of antibiotics, compared to the prescription across all general practitioners (16). The feedback given links results to guidelines on antimicrobial therapy. Another example – aimed at the general public this time - is the European Antibiotic Awareness Day, an annual event initiated in 2008 by the ECDC. This day is geared towards raising awareness about the risks associated with inappropriate use of antibiotics and how to take antibiotics responsibly (17).

Dutch usage of antimicrobials in humans is still sparse and targeted, and remains amongst the lowest in Europe (18). Guidelines from the Dutch Working Party on Antibiotic Policy (SWAB), the Dutch Working Party on Infection Prevention (WIP) and the Dutch Society of Family Physicians (NHG) play an important role in prescription behaviour. In addition, the Dutch Institute for Rational Use of Medicine (DGV) organises structured consultations between pharmacists and family physicians (4) and conducts scientific research (19). Rational prescriptive behaviour is the goal of these consultations.

Is there still room for improvement? Some settings (e.g. home care and possibly primary care) and some patient groups (children, the elderly) are not well represented in research. Moreover, guidelines on the use of antibiotics for specific settings as nursery homes and facilities for handicapped persons do not exist. Nursery homes are of particular interest as they seem a reservoir of AMR. They might even play a role in the spread (or continuous re-introduction) of AMR in different health care settings. In addition, new challenges lie in informal routes of acquiring antibiotics, such as over the counter purchases brought home by migrants and travellers, or purchases through the internet.

ZonMw acknowledges the importance of the concept of ‘good usage of drugs’ (goed gebruik van geneesmiddelen) after drug registration. The ‘good usage of drugs’ implies that (a) drugs are prescribed when needed and only then; (b) the correct drug is prescribed correctly; (c) the drug is used correctly by the patient. ZonMw has convened an expert meeting. ‘Good usage of drugs’ and research theme (5) have both strong links with the ZonMw programme Health Care Efficiency Research. Conclusions and recommendations of the expert meeting are available on request (22).

Research questions in this area include:

- Which interventions combine an optimum therapeutic effect with a minimal selection of resistance or with more favourable determinants of AMR?
- Is under-usage of antimicrobial therapy related to AMR?
- Does improved compliance result in less frequent emerging of resistant clones?
• What are the main determinants of prescribers’ adherence to guidelines, and which determinants can be influenced?
• What can we learn from interventions used in other countries?

5.5 Innovative approaches in antimicrobial resistance prevention

Innovative approaches to AMR control is much needed, both in health care settings as in the field of public health. Hand hygiene has been shown to be the single most effective way to prevent cross-transmission of microorganisms and protect patients. But compliance with hand hygiene amongst healthcare workers is quite low, at an estimated 40% (20).

Cross border approaches deserve attention. An example of a cross-border initiative is the MRSA-Net Project in which EUREGIO Münsterland (Germany) and Twente (the Netherlands) collaborate. The main aim of the project is to achieve a lower MRSA rate. A network of the major health care providers in the region was created. Activities of the network consist of: (a) synchronisation of MRSA guidelines and creation and testing of practicable and user friendly MRSA protocols, (b) training of staff in the health care service, (c) active information of the public in order to increase attention to infection prevention in general. To give another example of a project aimed at the general public we mention e-Bug here. E-Bug is funded by DG SANCO and is an internet learning tool on antibiotics and hygiene (hand washing) for junior and senior school children.

In health care settings alternatives to antimicrobials may be useful in the prevention of AMR infections. There are already several non-antimicrobial approaches to the treatment and prevention of non-resistant infection including probiotics, phages and phytomedicines. Phytomedicines that have been utilised include artemesunate for malaria, tea tree oil for skin infections, honey for wound infections, mastic gum for *H.pylori* gastric ulcers and cranberry juice for urinary tract infections (21).

Relevant research questions in this area include:
• Which lessons can be learned from cross-border projects?
• What is the impact of the new Public Health Act, which obliges doctors to report MRSA clusters, on the containment of MRSA?
• Which known alternatives to antimicrobials are useful in AMR prevention and control?
• Which are the best interventions directed at improving hygienic behaviour, e.g. hand washing?
• How (cost-) effective are infection prevention measures for infections caused by (multi-drug) resistant bacteria?
• How (cost-) effective are intervention strategies for the prevention of transmission of (multi-drug) resistant bacteria or resistance genes in different segments of the population?
• What are the effects of infection prevention control strategies on patient care?
6 Links to other initiatives

In Chapter 5 we have described initiatives with a direct link to one of the research areas. This chapter gives a brief overview of organisations that conduct activities or policy initiatives in the field of AMR control.

6.1 Dutch funding organisations

6.1.1 ZonMw

In parallel with the AMR research programme, ZonMw opens up two other research programmes for priority medicines in 2009: one targets medicines for children and one targets medicines for the elderly. The priority medicines for children programme has chosen infectious disease as one of the research themes. In addition, a programme on infectious disease and vaccines and a programme on infectious disease control are running at present. The efforts of ZonMw in the area of ‘good usage of drugs’ have been outlined in Section 5.4. An overview of related ZonMw projects is given in Section 12.4 in the Appendix.

6.1.2 NWO

In the fall of 2009 NWO opens the programme Centres for Systems Biology Research. Systems biology is an emerging and interdisciplinary research field. It aims to understand the dynamic interactions (a) between components of a living system, (b) between living systems mutually and (c) between living systems and their environment. Systems biology is an approach that uses integrating experiments in iterative cycles with computational modelling in order to answer biological questions. Modelling is not the final goal, but is a tool to increase understanding of the entire biological system.

A budget from the AMR research programme is available for projects that concern AMR, if a centre is awarded funding by NWO. ZonMw and NWO will collaborate closely for the AMR part of this programme.

6.1.3 WOTRO

WOTRO Science for Global Development is the division within NWO which supports scientific research on development issues, in particular poverty alleviation and sustainable development. WOTRO is funded by NWO and the Dutch Ministry of Foreign Affairs (BZ). WOTRO has identified four research themes based on internationally recognised research agendas related to the United Nations Millennium Development Goals.

One of these WOTRO themes – Global Health and Health Systems – is directed at research and knowledge transfer to contribute to achieving 3 Millennium Development Goals: (a) combat HIV/AIDS, malaria and other diseases; (b) reduce child mortality; and (c) improve maternal health. In line with this theme, WOTRO wishes to stimulate excellent research aimed at contributing to reducing the burden of
infectious diseases and antimicrobial resistance. Therefore, WOTRO has reserved 0.5 million Euros to contribute to development relevant research programmes submitted within ZonMw’s Antimicrobial Resistance research programme. For more information on the WOTRO contribution to the AMR programme, please see paragraph 8.4.5.

6.1.4 LNV
LNV will facilitate the realisation of the pacts sealed between animal husbandry organisations in the various production sectors, by co-funding the development and distribution of knowledge and development of monitoring instruments and systems. LNV intends to extend and up-scale the funding of the present research programme ALTANT, mentioned in Section 5.2. Thus, the market introduction of promising alternatives to antimicrobials can be facilitated. Moreover, it is likely that LNV will fund an innovation programme aiming at animal production chains using no or very limited amounts of antimicrobials.

6.2 Other Dutch organisations
Many Dutch organisations are involved in AMR research. Besides SWAB and WIP, mentioned in Sections 5.1 and 5.4, and the universities with their medical centres, we will briefly introduce FIGON, RIVM CIb and the professional societies here.

6.2.1 FIGON
The Netherlands Federation for Innovative Drug Research (FIGON) is an integrative platform for innovative drug research in the Netherlands. It enhances existing initiatives and signals new developments. ZonMw actively supports the activities of FIGON.

6.2.2 RIVM CIb
RIVM’s Centre for Infectious Disease Control (CIb) is involved in the AMR surveillance and MRSA research, as described previously. In addition, the CIb is setting up a surveillance system that will enable real time monitoring of health care AMR. This system will provide timely data to (a) detect and track AMR outbreaks across institutes; (b) to identify and track newly emerging AMR; (c) to give feedback to individual institutes for the purpose of quality control and AMR control. CIb is also involved in public campaigns on the correct use of antibiotics. And the CIb will examine the prevalence of the use of antibiotics in nursing homes, in collaboration with SWAB. Results of the program will be shared with the CIb for implementation.

6.2.3 Professional societies
Professional societies that are active in scientific research in the field of AMR are:
- VIZ (Society for Infectious Diseases)
- NVMM (Dutch Society for Medical Microbiology)
- NVZA (Dutch Society of Hospital Pharmacists)
- NHG (Dutch Society of Family Physicians)

6.3 International programmes and initiatives
In this section the main international initiatives are described.

6.3.1 ECDC
As mentioned in the introduction, the ECDC acknowledges AMR as one of the major threats related to infectious disease (9). It deploys many activities in relationship to AMR such as the before mentioned European Antibiotic Awareness Day. In addition, ECDC supports European (surveillance) networks, including:
- ESAC (European Surveillance of Antimicrobial Consumption) (www.esac.ua.ac.be/). The core of ESAC’s work is to maintain a database on antibiotic use in Europe. In addition, ESAC studies antibiotic usage in different settings such as hospitals or ambulatory care.
- EARSS (European Antimicrobial Resistance Surveillance System) (www.rivm.nl/earss)
- Med-Vet-Net is a network of excellence that integrates the medical, veterinary and food sciences. Part of the work of Med-Vet-Net is an investigation of AMR in bacterial strains from many sources along the food chain

6.3.2 DG SANCO
Projects related to AMR initiated by DG Sanco include:
- SCORE (Strategic Council on Resistance in Europe) (11)
- Antibiotic Strategies (ABS) International (www.abs-international.eu)
- Burden of Resistance and Disease in European Nations (www.eu-burden.info)

6.3.3 DG Research
Currently funded relevant projects include:
- Grace (Genomics to combat resistance against antibiotics in community-acquired lower respiratory tract infections) (www.grace-lrtri.org)
- CHAMP (Changing behaviour of health care professionals and the general public towards a more prudent use of antimicrobial agents) (CHAMP)
- MOSAR (Mastering Hospital Antimicrobial Resistance in Europe) (www.mosar-sic.org/mosar/en-GB/)

The most recent AMR projects funded under Framework Programme 7 are listed in Section 12.5 in the Appendix.
6.3.4 CDC

The United States´ Centre for Disease Control (CDC) deploys a range of AMR-related activities. To name a few: a national AMR surveillance system, a national campaign to prevent AMR in health care settings and several public campaigns (e.g. educational activities to promote appropriate use of antibiotics agents in animals).

6.3.5 WHO

The WHO has outlined a Global Strategy for the Containment of Antimicrobial Resistance. This strategy targets all areas where antimicrobials are used in the community, hospitals and agriculture. In collaboration with the United Nations Food and Agriculture Organization (FAO) and the Office International des Epizooties (OIE), global recommendations for antimicrobial use in agriculture are developed. In addition, WHO is enhancing food borne disease surveillance and antimicrobial resistance testing of food borne bacteria. The laboratory strengthening focuses on salmonellosis.

More information on WHO activities can be found under:
- WHO Drug Resistance Programme (www.who.int/drugresistance/en)
- Priority research topics
## 7 Communication and implementation

Three of the specific goals of the AMR research programme are (a) to stimulate knowledge transfer (b) to create the conditions necessary to implement research results and (c) to foster collaboration between research, policy and practice, animal and human health and public and private partners. These specific goals are a prerequisite to reach the programme’s more general aim: to contribute to the control of antimicrobial resistance, by stimulating research in the field of antibiotics’ use and the development of new medicines or interventions. Attention to communication and implementation is crucial to these three specific goals, both at project level and at programme level. This section outlines the most important aspects of communication and implementation of the AMR research programme.

### 7.1 Starting points

The specific goals and expected results, with regard to implementation and communication, have been outlined in Section 4 and in 12.3 in the Appendix. The following starting points have been formulated to achieve the specific goals and the expected results:

1. Communication with the sponsor
   The programme has a special relationship with its sponsors VWS and NWO. Communication takes place on a regular basis and concerns process, bottlenecks and (provisional) results.

2. Definition of the network
   An efficient communication and implementation policy requires a definition of the network in which the programme is rolled out. Relevant questions are: who is the sponsor? Who is the executive? Who is the policy maker? Who is the owner of this problem? How are communication channels organised? What are the gaps? Which fields have strong working relationships and in which fields further investment in collaboration is needed? What is the position of the programme within the network? What parties are involved in harmonisation? Who is in charge? Who will take over?

3. Active network responsibility
   The committee and the secretariat have an active responsibility in the network. At programme level, they are responsible for maintaining contact, making appointments, and channelling information and input from the field and policy makers towards ongoing projects.

4. Collaboration incentive
   The programme aims at active incentives for collaboration between research parties. Project proposals will be judged on collaboration efforts. If necessary, ZonMw can suggest potential partners to get acquainted, exchange information and harmonise their policy. ZonMw can use its communication tools to this extent and link up to existing channels of communication.
5. Successful implementation
With the midterm progress report the project manager has to respond to questions about knowledge transfer and implementation of the possible results of the project. This plan will be judged jointly with the progress report. At the end of the project, an evaluation will be held that examines the extent to which all intentions in the plan have been put to practice. In the case of a gap between plan and practice, activities that bridge this gap will be identified. After the finalisation of the project, ZonMw can follow up the implementation of the project for up to 4 years. In addition, ZonMw can support implementation activities.

6. Agreement of (end) users
Each project proposal describes how the research question and the project’s aim have been concerted with practice and policy makers. Where possible, the proposal describes what agreements have been made with future users of the project’s results. Anticipation of end results usage is a key element on which the project proposal is judged.

7. Transfer of programme results to educational programmes
ZonMw selects educational institutions for the delegation of knowledge from the programmes and defines concrete agreements for the use of programme results in educational programmes.

7.2 Methodology
The before mentioned starting points result in a methodology, with relevance to communication on project level as well as on programme level:

- Periodical meetings – project manager meeting, stakeholders meetings, expert meetings
- Progress reports and annual reports for the sponsors
- Incorporation of project information in the ZonMw database
- Distribution of news items and programme results through the an e-mail newsletter, Pre-Post, Mediator, scientific journals and the regional and national press
- Information through a sub site of the ZonMw website
- Progress reports and final reports
8 Organisation of the programme

This section discusses how the programme is to be organised and the procedures that will guarantee the quality, independence and relevance (to society and otherwise) of the research results.

8.1 The role of ZonMw

ZonMw works to strengthen health and healthcare. It does so by fostering and financing research, development and implementation. ZonMw has an independent position – in between research, policy and practice. Within its programmatic working method, the programme committee takes a central role.

8.2 The programme committee

The board of ZonMw has appointed a programme committee (12.6 in the Appendix). Members have been appointed in their personal capacity. Criteria in the selection process were:

- Knowledge of, experience with and affinity for the field of AMR
- Knowledge of and affinity for research
- Diversity of its members (e.g. background, working place, gender)

Observers from VWS, LNV and NWO (WOTRO) will be invited to committee meetings. The committee is responsible for formulating and executing the programme. Specific tasks of the committee are:

1. To formulate the AMR research programme and supplemental documents;
2. To contribute to locating additional funding;
3. To prioritise and award proposals;
4. To monitor and evaluate the programme and make adjustments where needed;
5. To contribute to communication efforts on the research programme Priority Medicines Antimicrobial Resistance, in order to enhance coherence and collaboration;
6. To contribute to the dissemination of results of the programme and to create the conditions necessary to bring these results into practice;
7. To foster and monitor the usage of knowledge gained.

ZonMw strongly feels that decision making should be as objective as possible and exercised by careful and transparent procedures. To do so, conflicts of interest – or even a hint thereof – are banned. To this purpose, ZonMw makes use of a code of conduct which is available in the public domain (http://www.zonmw.nl/fileadmin/cm/subsidiewijzer/documenten/Code_Belangenverstrengeling_ZonMw_engels.pdf). It is the responsibility of the bureau of ZonMw to apply this code correctly. In addition, the chair of the committee and the programme officer have the authority to withhold specific information from individual committee members. This concerns committee members involved –directly or indirectly – in proposals, where the specified information would give them an unfair advantage over non-committee members.
8.3 Working method

The research programme AMR intends to organise three calls for project ideas; one in September 2009, one in 2011 and one in 2012. A detailed timeline is included in Section 12.7 in the Appendix. Each call concerns all research areas: (1) The role of antimicrobial use in inducing and transmitting resistance; (2) Mechanisms and targets for new drugs; (3) New technologies, in particular rapid diagnostics; (4) Optimising antimicrobial therapy: dosage and use; (5) Innovative approaches in antimicrobial resistance prevention. For all research areas, the methodology of infectious disease modelling is considered of particular value. The discovery of new points of action for drugs or vaccines, is clearly a part of this research programme. The development of new drugs or vaccines has no place in the programme. The committee will focus the research areas in the subsequent calls following the submission of proposals on the first call.

Systems biology can contribute to the AMR programme in research area (2). Collaboration with NWO has created the opportunity to apply for funding of AMR related research within the programme Centres for Systems Biology Research. A call for proposals has been published at [www.nwo.nl](http://www.nwo.nl) and has closed September 8, 2009.

Overall, awarded projects will include all research areas and strike a balance between:

- Fundamental vs. applied research
- Research by (larger) consortia vs. individual (or smaller) groups
- Short-term vs. long-term research
- Research with a national perspective vs. an international perspective, linked to research areas in the EU seventh Framework programme and to the research agenda of the ECDC

The number of awarded projects and the number of projects awarded per research area will be coordinated by the programme committee, and depends upon the available budget.

Within ZonMw, the AMR programme will align its working method with other ZonMw programmes if necessary. This concerns the other two programmes on priority medicines (children and the elderly) with a call in 2009. In addition, the AMR programme will seek - and continue already existing - collaboration with external parties, such as WOTRO, LNV and others. A joint call or programming study is considered a future effort.

8.4 Procedures

ZonMw has established procedures to evaluate proposals for all its programmes. A description of ZonMw’s procedures is available in the brochure ‘Procedures voor ZonMw-programma’s’ (in Dutch) at [www.zonmw.nl](http://www.zonmw.nl). Alternatively order by mail (info@zonmw.nl) or by phone: +31 (0)70 3495111.

The AMR programme committee determined the overall procedures and working methods of the AMR programme on its first meeting in August 2009. The committee will set out more detailed procedures
following the submission of proposals on the first call. At that time the exact weighing of the quality and relevance of project proposals will be determined as well.

8.4.1 General procedures concerning proposals

The committee will decide to stimulate bottom-up and/or top-down research, dependent on the principal research theme and the financing institution. There are 7 steps in the evaluation of proposals:

1. Call for project ideas: ZonMw places a call on its website, in Mediator and professional media if needed. The call requests interested parties to submit project ideas within 8 weeks.
2. Evaluation of project ideas: mainly based on relevance and broadly on research quality
3. Call for proposals: ZonMw will invite researchers of selected project ideas to submit a detailed proposal
4. External review and comment round: each detailed proposal will be refereed by two or more independent reviewers. Reviewers are selected from different fields of expertise and may differ in their opinions. Submitters can respond in writing to the anonymous reviews
5. Quality evaluation: the programme committee will make a final evaluation on the quality of submitted proposals, based on the anonymous reviews and the written response of the submitter
6. Evaluation of relevance and prioritization: the programme committee makes a final judgement on the relevance of the proposed research and prioritises proposals based on both relevance and quality. For the method of prioritising please see example 2 in the brochure Procedures.
7. The reward or rejection of submitted proposals: the committee advises the board of ZonMw on the reward or rejection of submitted proposals. On behalf of the board ZonMw’s CEO will inform submitters of the boards final decision

8.4.2 Criteria to evaluate relevance

The relevance criteria mentioned here below are intended to inform submitters as well as the programme committee. In addition, submission forms are designed so as to encourage submitters to explicitly demonstrate the relevance of the project by using the relevance criteria.

1. Contribution of the submitted project to aims and goals of the programme: does the project fit within the general and specific scope of the programme, and does it contribute to its aims?
2. Innovative: is this an innovative project? Does the project generate new insights?
3. Public and or scientific interest: does the project meet public needs? Does the project address knowledge gaps?
4. Costs and benefits: does the project strike a balance between effort, input and means on the one hand and (expected) results and impact on the other hand?

5. Attention to gender, culture, age, the patient’s perspective and specific risk groups. ZonMw considers attention to these aspects crucial and includes them in to the evaluation of a project’s relevance. Proposals have to define why they do or do not give attention to these aspects with referees to support.

6. Attention to dissemination of results and the implementation of a project’s results. Attention to the further use of a project’s output is part of any research project. For projects in which development is an important part, attention to the further use of a project’s output will be part of the evaluation of a project’s relevance and quality. The criteria used to evaluate the dissemination and implementation of project results may differ along project type. Aspects for evaluation can be:
   a. Is there an adequate strategy for the dissemination and implementation of results?
   b. Are stake-holders user-groups well defined?
   c. Are such groups actively involved in the project?
   d. What specific activities are scheduled?
   e. Are the right people and/or groups involved in these activities?

8.4.3 Criteria to evaluate quality

ZonMw has laid down general criteria to evaluate the quality of submitted projects:

1. Objective, problem definition and/or assignment
   Original projects with scope and a clear objective are what is looked for. An objective must be clear and specific. Research objectives need a specific and verifiable research question. In projects concerned with development and implementation the assignment needs to be clearly defined, practical and consistent with a broader objective. Scope is of importance: how important is the subject, what is the theoretical or empirical evidence presented in support of the problem definition/assignment and does the project add value to existing knowledge or practice? A proposed project may not be a repetition of any (running) project

2. Strategy
   The strategy is clear and suffices to carry out the project. It describes the methods and analyses supported by a theoretical or empirical framework. If there is a target group, the strategy defines how gender, culture, age, and specific risk groups are reflected in the project. In addition, the degree of collaboration with intermediate and/or ultimate target groups (the patient/client perspective) is outlined here.
3. Project group
Factors associated with a successful project group can include relevant experience, familiarity with the area in question and prior activities and projects. Publications, guidelines and interventions and the number and nature of grants received as well as (international) contacts with peers and target groups may reflect a group’s success. Notwithstanding, promising new talent stands a good chance to secure funding of their proposal.

4. Feasibility
It should be likely that a project’s objective or assignment can be achieved with the proposed strategy and with the available and/or requested means, staff and facilities. A timeline must be realistic. Projects need to pay attention to any factors that may impede or facilitate the process.

5. Development and implementation projects: attention to the dissemination and implementation of results

8.4.4 Specific criteria Priority Medicines Antimicrobial Resistance
Some criteria are specific to the programme and will assist prioritise proposals:

1. Projects that are embedded in wider (regional) networks with the following key elements:
   a. Collaboration between municipal health services, health care providers, universities and/or knowledge centres
   b. Coherence at a national level
   c. Interaction between research, teaching and practice
   d. Research led by real life problems
   e. Output (products and services) based on science and with a use in practice

2. Projects in all research areas are funded. For all research areas, the methodology of infectious disease modeling is considered of particular value.

3. Attention to collaboration. Collaboration within projects is considered crucial. The concrete nature of the collaboration and its sustainability will be part of the evaluation of a project. Academic Collaborative Centres are an example of long-term partnerships - here between community health centres and universities – facilitated by ZonMw. These Centres strengthen research activities in the public health sector and improve knowledge transfer between practitioners, policymakers, researchers and the educational sector. Where possible, projects should link up with the Academic Collaborative Centres.
   http://www.zonmw.nl/nl/onderwerpen/alle-programma-s/academische-werkplaatsen-publieke-gezondheid/

4. Attention to European and international research agendas and to international collaboration.
Is international collaboration relevant for the proposed project or not? Are similar projects undertaken abroad and can researchers link up or learn lessons from these projects? In particular, collaboration with partners in ‘endemic’ countries in e.g. Eastern and Southern Europe may be of relevance. It is evident that project proposals should not overlap with any existing research project. Project proposals may however link with existing projects that receive international funding. It is a prerequisite that such a proposal is a logical next step, originating from, but very much independent to, the existing research project.

8.4.5 Additional criteria WOTRO

WOTRO has reserved 0.5 million Euros to contribute approximately 2 to 5 development relevant research programmes submitted within the Priority Medicines Antimicrobial Resistance programme. The same budgetary conditions apply as for the main AMR programme, as mentioned in paragraph 8.3. The WOTRO budget will be used to fund parts of applications addressing a health problem relevant for a developing country or region and including that developing country or region. The relevance of proposed research for the local problem should be clearly explained in the proposal. In addition to the general ZonMw and specific AMR quality and relevance criteria, the proposal must be a collaborative initiative of researchers from the Netherlands and from one or more developing countries¹ (DC) to qualify for WOTRO funds. DC partner institutions and DC researchers have to be involved in the formulation of the research questions and the development of the proposal as well as in carrying out the research programme. The main applicant should be a senior researcher employed by a NWO recognised grant recipient or by an international centre for scientific education based in the Netherlands. A senior researcher from the partner organisation in the developing country concerned with a PhD degree should be the co-applicant and a member of the coordinating team. The research team must include post-doc or PhD researchers originating from a developing country with a minimum of one DC researcher.

To enhance effective use, the uptake of results and the benefit for society, relevant stakeholders from outside the scientific community are expected to be engaged in all phases of the programme, from its inception to sharing emerging results. A communication plan directed at the preparation, uptake, translation and application of relevant research issues and results with stakeholders from outside traditional scientific communities must be part of the research programme.

¹ Developing countries include all low and middle-income non-EU countries that qualify for receiving Official Development Assistance (ODA), as defined by the OECD (see www.oecd.org/dac/stats/daclist)
9 Monitoring and evaluation

The progress of the programme is monitored by the programme committee.

9.1 Projects’ progress

The progress of awarded research projects is monitored by the programme committee and based on a midterm progress reports and final reports submitted by the project managers. The programme committee evaluates whether the project is on schedule, based on the original project proposal. In addition, they assess whether the project needs amendments or adjustments. The committee focuses specifically on how researchers promote the implementation of the research results. After the completion of a project, ZonMw actively follows the project up for 1 up to 4 years on the progress of the dissemination of results and the implementation of the project’s results.

9.2 Progress of the programme

The programme committee keeps sponsors and potential users posted on the progress of the programme through means of an annual progress report. Primary focus of the report is to describe how programme activities have contributed to programme targets. The expected results and verifiable indicators that were outlined in Sections 4 and 12.3 in the Appendix will be used in this context. These reports give the programme committee and sponsors all relevant information to adjust the programme, if necessary.

9.3 Evaluation of the programme

The programme runs from 2009 until 2018 and can be expanded depending on potential sponsors. The programme committee evaluates the programme once during the term of the programme and once after the conclusion of the term. Evaluation is based on granting criteria and performance indicators decided upon, together with the sponsors, prior to the start of the programme. The evaluation focuses on programme priorities, working methods and procedures, results, time schedule and budget. The results of the evaluation are described in a programme report that is presented to the sponsors.
## 10 Funding structure

### Budget

<table>
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<tr>
<th>Category</th>
<th>Amount</th>
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<tr>
<td>Projects</td>
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<tr>
<td>Communication and implementation</td>
<td>€700,000</td>
</tr>
<tr>
<td>General costs</td>
<td>€100,000</td>
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<td>Committee</td>
<td>€86,500</td>
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<td>Programme costs</td>
<td>€1,358,550</td>
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<td><strong>Total</strong></td>
<td><strong>€14,760,000</strong></td>
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### Budget projects

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<tr>
<th>Round</th>
<th>Percentage</th>
<th>Amount</th>
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</thead>
<tbody>
<tr>
<td>First round</td>
<td>50%</td>
<td>€6,257,475</td>
</tr>
<tr>
<td>Second round</td>
<td>30%</td>
<td>€3,754,485</td>
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<tr>
<td>Third round</td>
<td>20%</td>
<td>€2,502,990</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td><strong>€12,514,950</strong></td>
</tr>
</tbody>
</table>

The projects budget includes 1M € for Centres for Systems Biology Research.

On top of the projects budget there is €500,000 available from WOTRO Science for Global Development to development relevant research projects.
## 11 Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABRES</td>
<td>Interdepartmental Platform Antibiotic Resistance</td>
</tr>
<tr>
<td>ALTANT</td>
<td>Alternatives for the problem of antimicrobial resistance in animal husbandry</td>
</tr>
<tr>
<td>AMR</td>
<td>Antimicrobial Resistance</td>
</tr>
<tr>
<td>BZ</td>
<td>Dutch Ministry of Foreign Affairs</td>
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<tr>
<td>CEO</td>
<td>Chief Executive Officer</td>
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<tr>
<td>CDC</td>
<td>Centre for Disease Control</td>
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<tr>
<td>Clb</td>
<td>Centre for Infectious Disease Control Netherlands</td>
</tr>
<tr>
<td>CSBR</td>
<td>Centres for Systems Biology Research</td>
</tr>
<tr>
<td>CTMM</td>
<td>Center for Translational Molecular Medicine</td>
</tr>
<tr>
<td>CVI</td>
<td>Central Veterinary Institute</td>
</tr>
<tr>
<td>DG</td>
<td>Dutch Institute for Rational Use of Medicine</td>
</tr>
<tr>
<td>ECDC</td>
<td>European Centre for Disease Control</td>
</tr>
<tr>
<td>EARSS</td>
<td>European Antimicrobial Resistance Surveillance System</td>
</tr>
<tr>
<td>EASAC</td>
<td>European Academies Science Advisory Council</td>
</tr>
<tr>
<td>ESAC</td>
<td>European Surveillance of Antimicrobial Consumption</td>
</tr>
<tr>
<td>ESBL</td>
<td>Extended spectrum beta lactamase</td>
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<tr>
<td>FIGON</td>
<td>Netherlands Federation for Innovative Drug Research</td>
</tr>
<tr>
<td>GD</td>
<td>Animal Health Service Deventer</td>
</tr>
<tr>
<td>GGD</td>
<td>Institutes for Public Health Services</td>
</tr>
<tr>
<td>GR</td>
<td>Health Council of the Netherlands</td>
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<tr>
<td>KNAW</td>
<td>Royal Netherlands Academy of Arts and Sciences</td>
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<tr>
<td>KNCV</td>
<td>Dutch Tuberculosis Foundation</td>
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<tr>
<td>LNV</td>
<td>Ministry of Agriculture, Nature and Food Quality</td>
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<tr>
<td>MARAN</td>
<td>Monitoring of Antimicrobial Resistance and Antibiotic Usage in Animals in the Netherlands</td>
</tr>
<tr>
<td>MRSA</td>
<td>Methicillin-resistant <em>S. aureus</em></td>
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<tr>
<td>NHG</td>
<td>Dutch Society of Family Physicians</td>
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<tr>
<td>NIVEL</td>
<td>Netherlands Institute for Health Services Research</td>
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<tr>
<td>NWO</td>
<td>Netherlands Organisation for Scientific Research</td>
</tr>
<tr>
<td>RGO</td>
<td>Advisory Council on Health Research</td>
</tr>
<tr>
<td>RIVM</td>
<td>National Institute for Public Health and the Environment</td>
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<tr>
<td>SCORE</td>
<td>Strategic Council on Resistance in Europe</td>
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<tr>
<td>SWAB</td>
<td>Dutch Working Party on Antibiotic Policy</td>
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<tr>
<td>Ti Pharma</td>
<td>Top Institute Pharma</td>
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<tr>
<td>VANTURES</td>
<td>Veterinary Antibiotic Usage and Resistance Surveillance Working Group</td>
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<tr>
<td>VWA</td>
<td>Food and Consumer Product Safety Authority</td>
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<tr>
<td>VWS</td>
<td>Ministry of Health, Welfare and Sport</td>
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<td>WHO</td>
<td>World Health Organisation</td>
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<tr>
<td>WIP</td>
<td>Dutch Working Party on Infection Prevention</td>
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<tr>
<td>WOTRO</td>
<td>Science Division NWO which supports scientific research on development issues</td>
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<tr>
<td>ZonMw</td>
<td>The Netherlands organisation for health research and development</td>
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12 Appendices
12.1 Letter VWS concerning the Priority Medicines Antimicrobial Resistance Programme

Ministerie van Volksgezondheid, Welzijn en Sport

Zonhoven
T.s.v. het bestuur
Postbus 93245
2500 AE DEN HAAG

Onderwerp:
Gezondheids- en de veeteelt op het programmeergeleid
Antimicrobiële Resistente

10 oktober 2008

In de loop der jaren heeft een aantal micro-organismen resistentie ontwikkeld tegen antibiotica die eerder wel effectief waren. Specifieke beleidstaken van het VWS zijn er: de resistentie tegen MRSA (methicilline resistentie Staphylococcus aureus) en de resistente tegen geneesmiddelen voor melkvee en zuivelfeit. Tegenslagen van resistente en de ontwikkeling van nieuwe middelen en methoden om resistente te voorkomen is niet in staat (weer)staakt. Het bestuur van het VWS heeft om deze redenen besloten om een bijdrage te leveren aan het bemiddelen en om de nieuwe geneesmiddelen (MEG) te begeleiden. Het VWS heeft deze keuze gemaakt en om de nodige middelen te beschikbaar te stellen.

In de loop der jaren heeft een aantal micro-organismen resistentie ontwikkeld tegen antibiotica die eerder wel effectief waren. Specifieke beleidstaken van het VWS zijn er: de resistentie tegen MRSA (methicilline resistentie Staphylococcus aureus) en de resistente tegen geneesmiddelen voor melkvee en zuivelfeit. Tegenslagen van resistente en de ontwikkeling van nieuwe middelen en methoden om resistente te voorkomen is niet in staat (weer)staakt. Het bestuur van het VWS heeft om deze redenen besloten om een bijdrage te leveren aan het bemiddelen en om de nieuwe geneesmiddelen (MEG) te begeleiden. Het VWS heeft deze keuze gemaakt en om de nodige middelen te beschikbaar te stellen.

De problemen van de resistentie van sommige bacteria tegen antibiotica worden deels veroorzaakt door het veelvuldig gebruik van antibiotica in de veehouderij. Bij de voorbereidende verkenningen die geleden zijn heeft dit programma een deel van de vraagstukken met behulp van middelen en methoden om resistente te voorkomen. Het VWS heeft deze keuze gemaakt en om de nodige middelen te beschikbaar te stellen.
Ik verzoek u bij het uitzetten van aanvragen voor het indienen van projectvoorstellen ('calls for proposals') aandacht te besteden aan deze problematiek. In het bijzonder vraag ik u te bezien of het onderzoek dat betrekking heeft op thema 2 inhoudelijk i thematisch aan kan sluiten bij het door de ministerie van LNV voorgenomen onderzoek naar alternatieven voor antibiotica in de diergeneeskunde. U kunt hiervoor contact opnemen met Ohr. A. Moliering, directeur Vealieduwijk en Gezondheidszorg van het ministerie van LNV staal 070-3784338, e-mail: amoliering@milv.nl.

De directeur GMT (Ohr. H. Sierweg) en de directeur PG (mmr. F. van Rial) zouden graag als waarnemer deel uitmaken van de jury voor dit programma aan te trekken deelcommissie. Ook verzoeken wij u aan gaafdat Bij het ministerie van LNV op te nemen in deze commissie.

Ik ga er van uit dat u de hieronder aangegeven projecten per thema, zoals u in uw voorlopige aanpassing toestemt, aanslaat voor de commissie van wetenschappelijke kwaliteit en relevantie en de criteria voor toekenning en haalbaarheid.

Om uitvoering te geven aan de vijf thematische stelt ik de volgende financiële middelen voor beschikking van in totaal € 14.780.000.000. Het hieraan verbonden kasteel ziet ik volgen en volgende uitgevoerde programma als volgt:

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<td>110</td>
<td>14.780</td>
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Vooral verzoek ik in de eervolgende (voorlopige) rapportage dit programma danwel inhoudelijk of financier moet te nemen.

Hierop zal ik het uitgeven van het verplichtingsbijlond verhogen en ontvangt u een aanvullend schijven op mijn brief d.d. 20 december 2007 (Kamerx 82,821,810) en n.l. 8 juli 2008 (KG/BR 2,281,281) inzake de goedkeuring van de begroting van het jaarplan 2008.

Ten slotte zijn de wetenschappelijke planning & controle VWS, WWI en ZWU van toepassing.


Ik hoop dat u hiervan niets voldoende heeft kunnen informeren en ik welke u succes bij de uitvoering van dit programma.

De minister-generaal van de Vlaamse overheid.
### 12.2 Consulted experts

<table>
<thead>
<tr>
<th>Name</th>
<th>Organisation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dr. W.P. Achterberg</td>
<td>Verpleeghuis Houtens Erf, Houten</td>
</tr>
<tr>
<td>Dr. M.J. Bakker</td>
<td>GGD Den Haag</td>
</tr>
<tr>
<td>Prof. Dr. M.J.M. Bonten</td>
<td>Universitair Medisch Centrum Utrecht</td>
</tr>
<tr>
<td>Prof. Dr. M.W. Borgdorff</td>
<td>Academisch Medisch Centrum, Amsterdam</td>
</tr>
<tr>
<td>Prof. P.J. van den Broek</td>
<td>Universitair Medisch Centrum Leiden</td>
</tr>
<tr>
<td>Prof. dr. H.J.M. Cools</td>
<td>Universitair medisch Centrum Leiden</td>
</tr>
<tr>
<td>Prof. Dr. D.J.A. Crommelin</td>
<td>TI Pharma</td>
</tr>
<tr>
<td>Prof. Dr. J.E. Degener</td>
<td>Universitair Medisch Centrum Groningen</td>
</tr>
<tr>
<td>Prof. Dr. J.T. van Dissel</td>
<td>Universitair Medisch Centrum Leiden</td>
</tr>
<tr>
<td>Dr. B.W.K. Ganter</td>
<td>WHO, Geneve</td>
</tr>
<tr>
<td>Prof. Dr. H. Grundmann</td>
<td>RIVM, Bilthoven</td>
</tr>
<tr>
<td>Prof. dr. A.P. Hardon</td>
<td>Universiteit van Amsterdam</td>
</tr>
<tr>
<td>Prof. J.A.P. Heesterbeek</td>
<td>Universiteit Utrecht</td>
</tr>
<tr>
<td>Dhr. R. Hendrix</td>
<td>Medisch Spectrum Twente</td>
</tr>
<tr>
<td>Mw. J. van Hout</td>
<td>De Gezondheidsdienst voor Dieren</td>
</tr>
<tr>
<td>Dhr. P. Jacobs</td>
<td>GGD Zuid-Limburg</td>
</tr>
<tr>
<td>Drs. J.H.T.C. van den Kerkhof</td>
<td>RIVM Bilthoven</td>
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<tr>
<td>Drs. R.P.M. van Kessel</td>
<td>GGD Eemland</td>
</tr>
<tr>
<td>Prof. Dr. J. Kluytmans</td>
<td>VU medisch centrum, Amsterdam</td>
</tr>
<tr>
<td>Dr. M. Kretzschmar</td>
<td>Universitair Medisch Centrum Utrecht</td>
</tr>
<tr>
<td>Mw. A. Lonroth</td>
<td>EC Europe</td>
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<tr>
<td>Dr. D.J. Mevius</td>
<td>WUR</td>
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<tr>
<td>Mw. D. Monnet</td>
<td>ECDC</td>
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<tr>
<td>Dr. B. Mulder</td>
<td>Streeklaboratorium Twente</td>
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<tr>
<td>Dr. J.M. Prins</td>
<td>AMC UVA / SWAB</td>
</tr>
<tr>
<td>Prof. Dr. P. Speelman</td>
<td>Academisch Medisch Centrum</td>
</tr>
<tr>
<td>Prof. Dr. L.J.J.M. Steeghs PhD</td>
<td>Immunovalley</td>
</tr>
<tr>
<td>Dr. E.E. Stobberingh</td>
<td>Academisch ziekenhuis Maastricht</td>
</tr>
<tr>
<td>Mw. A. Timen</td>
<td>RIVM, Bilthoven</td>
</tr>
<tr>
<td>Prof. Dr. C.M.J.E. Vandenbroucke</td>
<td>VU medisch centrum, Amsterdam</td>
</tr>
<tr>
<td>Prof. Dr. J.W.M. van der Meer</td>
<td>UMC St. Radboud, Nijmegen</td>
</tr>
<tr>
<td>Prof. Dr. H.A. Verbrugh</td>
<td>Erasmus Medisch Centrum, Rotterdam</td>
</tr>
<tr>
<td>Prof. Dr. Th.J.M. Verheij</td>
<td>Universitair Medisch Centrum Utrecht</td>
</tr>
<tr>
<td>Prof. A. Vermeulen</td>
<td>Immunovalley</td>
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<tr>
<td>Prof. dr. J.A. Wagenaar</td>
<td>Universiteit Utrecht</td>
</tr>
<tr>
<td>Dhr. P. Wever</td>
<td>Gezondheidsdienst voor Dieren</td>
</tr>
<tr>
<td>Prof. dr. B. van der Zeyst</td>
<td>Nederlands Vaccin Instituut, Bilthoven</td>
</tr>
</tbody>
</table>
### 12.3 Programme objectives, results and indicators

#### Matrix of programme’s objectives, expected results and verifiable indicators

<table>
<thead>
<tr>
<th>General objective</th>
<th>Specific objectives</th>
<th>Expected results</th>
<th>Verifiable indicators</th>
</tr>
</thead>
<tbody>
<tr>
<td>To contribute to the control of antimicrobial resistance by facilitating and stimulating scientific research</td>
<td>To further our understanding of the role of antimicrobial use in inducing and transmitting resistance</td>
<td>Proposals have been awarded and research projects have started</td>
<td>Number of completed projects</td>
</tr>
<tr>
<td></td>
<td>To help identify mechanisms and targets for new antimicrobial drugs or vaccines</td>
<td>Mechanisms and targets for new antimicrobial drugs or vaccines have been identified</td>
<td>Number of completed projects</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Collaboration with pharmaceutical partners has been established to further develop the insights gained</td>
<td>Number of projects adjusted with private partners</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Number of projects with collaboration with private partners</td>
<td></td>
</tr>
<tr>
<td></td>
<td>To facilitate the development of new techniques in the control of antimicrobial resistance, in particular rapid diagnostics</td>
<td>New techniques in the control of antimicrobial resistance have been developed</td>
<td>Number of completed projects</td>
</tr>
<tr>
<td></td>
<td></td>
<td>New rapid diagnostics have been developed</td>
<td>Number of new rapid diagnostics developed</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Collaboration with private partners has been established to further develop the insights gained</td>
<td>Number of projects developed</td>
</tr>
<tr>
<td></td>
<td>To contribute to optimising antimicrobial therapy both in dosage and in use</td>
<td>Proposals have been awarded</td>
<td>Number of completed projects</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Research in to patients’ compliance and physicians’ adherence to guidelines has started</td>
<td>Number of guidelines and/or protocols that have been adapted or developed</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Number of guidelines and/or protocols that have been evaluated</td>
<td></td>
</tr>
<tr>
<td></td>
<td>To stimulate innovative preventive measures to be used in infectious disease control</td>
<td>Proposals have been awarded</td>
<td>Number of completed projects</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Number of implemented projects</td>
<td></td>
</tr>
<tr>
<td></td>
<td>To stimulate a systematic and overarching approach in AMR control</td>
<td>Proposals that include infectious disease modelling have been awarded</td>
<td>Number of completed projects that have used infectious disease modelling</td>
</tr>
<tr>
<td>Specific objectives</td>
<td>Expected results</td>
<td>Verifiable indicators</td>
<td></td>
</tr>
<tr>
<td>------------------------------------------------------------------------------------</td>
<td>-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td></td>
</tr>
</tbody>
</table>
| To stimulate knowledge transfer and to create the conditions necessary to implement research results | Projects’ results have been disseminated in the scientific community, in the field of infectious disease control and to end users when applicable  
Project leaders have made concrete contributions to the transfer of knowledge | Number of guidelines and/or protocols that have been adapted or developed  
Number of projects presented at symposia or congresses  
Number of articles published in journals  
Number of projects that disseminated results in another way e.g. through the popular media  
Number of projects with results incorporated in training programmes e.g. of health staff |
| To foster collaboration between (a) research, policy and practice; (b) animal and human health; and (c) public and private partners. In addition, to foster international collaboration especially with countries in Eastern and Southern Europe | Collaboration has been established within projects or between projects  
Partnerships have been formed or strengthened  
Strategic alliances have been build | Number of projects in which collaboration was established  
Number of projects with collaboration between the animal and human health sector  
Number of public-private partnerships that has been formed or strengthened  
Number of projects with international collaboration  
Number of contacts with partners (programme committee) |
12.4 Related ZonMw projects

**Thema 1  Ontstaan van resistentie en transmissie**

<table>
<thead>
<tr>
<th>Projecttitel</th>
<th>Hoofdaanvrager Organisatie</th>
<th>Programma</th>
<th>Setting Doelgroep</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antivirale resistentie bij herpes simplex virus</td>
<td>Dr. Boucher UMCU</td>
<td>Preventie 1</td>
<td></td>
</tr>
<tr>
<td>Combating antibiotic resistance by integrating molecular biology and mathematical modelling</td>
<td>Prof. dr. Bonten UMCU</td>
<td>Vici</td>
<td>Intramuraal</td>
</tr>
<tr>
<td>Resistance to beta-lactam antibiotics due to ESBL in the Netherlands. The REBEL-study</td>
<td>Prof. Vandenbroucke VUMC</td>
<td>Infectieziekte Bestrijding</td>
<td>Intramuraal Patiënten en huisgenoten</td>
</tr>
<tr>
<td>Marokko: Helicobacter pylori: prevalentie, virulentie, antibioticaresistentie bij Marokkaanse kinderen in Marokko, proefscrewing bij een asymptomatische populatie Marokkaanse kinderen</td>
<td>Drs. Dahhan Stichting PaceMaker in Global Health Drs. Chegary UvA</td>
<td>Cultuur en Gezondheid</td>
<td>Intramuraal Marokkaanse kinderen</td>
</tr>
<tr>
<td>HIV resistance despite modern high genetic barrier drugs: through the needle’s eye</td>
<td>Dr. Nijhuis UMCU</td>
<td>Vidi</td>
<td>Patiënten</td>
</tr>
<tr>
<td>Mechanisms of pattern recognition and innate resistance against Candida albicans infection</td>
<td>Prof. dr. Netea UMC Radboud</td>
<td>Vidi</td>
<td>Intramuraal Patiënten</td>
</tr>
</tbody>
</table>

**Thema 2  Mechanisme en targets voor nieuwe geneesmiddelen**

<table>
<thead>
<tr>
<th>Projecttitel</th>
<th>Hoofdaanvrager Organisatie</th>
<th>Programma</th>
<th>Setting Doelgroep</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mechanisms of pattern recognition and innate resistance against Candida albicans infection</td>
<td>Prof. dr. Netea UMC Radboud</td>
<td>Vidi</td>
<td>Intramuraal Patiënten</td>
</tr>
<tr>
<td>De adenosine-receptor als nieuw farmacologisch aangrijpingspunt in de behandeling van sepsis</td>
<td>Prof. dr. Smits UMC Radboud</td>
<td>Agiko-stipendia</td>
<td></td>
</tr>
</tbody>
</table>

**Thema 3  Nieuwe technologische ontwikkelingen**

<table>
<thead>
<tr>
<th>Projecttitel</th>
<th>Hoofdaanvrager Organisatie</th>
<th>Programma</th>
<th>Setting Doelgroep</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antivirale resistentie bij herpes simplex virus</td>
<td>Dr. Boucher UMCU</td>
<td>Preventie 1</td>
<td></td>
</tr>
<tr>
<td>Antimicrobial salivary peptides to reduce biofilm formation on silicone rubber valve prostheses of laryngectomized patients</td>
<td>Prof. dr. ir. Busscher UMCG</td>
<td>Agiko-stipendia</td>
<td>Intramuraal</td>
</tr>
</tbody>
</table>
## Thema 4 Optimalisering van antibioticatherapie

<table>
<thead>
<tr>
<th>Projecttitel</th>
<th>Hoofdaanvrager</th>
<th>Programma</th>
<th>Setting</th>
<th>Doelgroep</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optimaliseren van het voorschrijven van antibiotica bij <em>luchtweg aandoeningen</em> in de huisartspraktijk; preventie van resistentie van micro-organismen in de extramurale zorg, reductie van kosten en preventie van bijwerkingen.</td>
<td>Dr. Kuyvenhoven UMCU</td>
<td>Preventie 1</td>
<td>Huisartsen praktijk</td>
<td>Huisartsen</td>
</tr>
<tr>
<td>Het optimaliseren van het voorschrijven van antibiotica bij <em>luchtweginfecties</em> in de huisartsenpraktijk: regionale implementatie, effectiviteit, bestendiging en kosteneffectiviteit van een meervoudige interventie(ARTI-3)</td>
<td>Ir. Schouten MPA DGV</td>
<td>Preventie 2</td>
<td>Huisartsenpraktijk</td>
<td>Huisarts Farmacie</td>
</tr>
<tr>
<td>RCT of point of care C-reactive protein test and enhanced communication skills for managing acute cough due to <em>lower respiratory tract infection</em> in general practice: cost effectiveness and effect on diagnostic testing, antibiotic prescribing and recovery.</td>
<td>Prof. dr. Dinant MUMC</td>
<td>Doelmatigheids onderzoek</td>
<td>Huisartsenpraktijk</td>
<td>Eerstelijnszorg</td>
</tr>
<tr>
<td>Decision support for antimicrobial treatment of <em>pneumonia</em> in intensive care (ICEA study: Intensive Care, Expert system and Antimicrobial treatment)</td>
<td>Prof. dr. Hoepelman UMCU</td>
<td>Preventie 1</td>
<td>Intramuraal</td>
<td>Artsen IC</td>
</tr>
<tr>
<td>Compliance met antiretrovirale combinatietherapie voor <em>HIV</em>-seropositive druggebruikers in het verzorgingsgebied van de CAD Oostelijk Zuid-Limburg.</td>
<td>Prof. dr. Kok UniMaas</td>
<td>Preventie 1</td>
<td>Intramuraal</td>
<td>Risicogroep alcohol/ drugs</td>
</tr>
<tr>
<td>Beslissingsondersteuning op basis van grid technologie bij de behandeling van <em>HIV</em> geneesmiddelenresistentie</td>
<td>Dr. van der Vijver Erasmus MC</td>
<td>ICT en Disease Management</td>
<td>Intramuraal</td>
<td>Zorgverlener</td>
</tr>
<tr>
<td>Welke kinderen met <em>acute otitis media</em> hebben baat bij behandeling met antibiotica: een meta-analyse met individuele data van gerandomiseerde trials</td>
<td>Dr. Rovers UMCU</td>
<td>Alledaagse Ziekten</td>
<td>Huisartsenpraktijk</td>
<td>Kinderen</td>
</tr>
<tr>
<td>Prevention of antimicrobial resistance in hospitals: promoting appropriate use of antibiotics in hospital departments of <em>internal medicine</em></td>
<td>Dr. Hulscher* UMC Radboud</td>
<td>Preventie 1</td>
<td>Intramuraal</td>
<td>Artsen</td>
</tr>
<tr>
<td>Shorter treatment duration of <em>endocarditis</em> based on C-reactive protein values</td>
<td>Prof. dr. Speelman* AMC</td>
<td>Doelmatigheids onderzoek</td>
<td>Intramuraal</td>
<td>Patiënten cardiologie</td>
</tr>
<tr>
<td>Implementatie van intraveneuze toediening van antimicrobiële geneesmiddelen thuis</td>
<td>Dr. Dijkstra TNO</td>
<td>Thuiszorg</td>
<td>Thuiszorg</td>
<td>Patiënten</td>
</tr>
</tbody>
</table>

* = projectleider
## Thema 5 Infectieziektepreventie maatregelen: nieuwe benaderingen

<table>
<thead>
<tr>
<th>Projecttitel</th>
<th>Hoofdaanvrager Organisatie</th>
<th>Programma</th>
<th>Setting Doelgroep</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHIPS: chirurgische profylaxe en surveillance</td>
<td>Dr. Gyssens Erasmus MC</td>
<td>Preventie 1</td>
<td>Intramuraal Chirurgische patiënten</td>
</tr>
<tr>
<td>Orofaryngeale decontaminatie met chloorhexidine en chloorhexidine/colistine ter preventie van ventilator-geassocieerde pneumonie bij beademde Intensive Care patiënten.</td>
<td>Dr. van der Ven UMC Radboud</td>
<td>Preventie 1</td>
<td>Intramuraal Beademde IC patiënten</td>
</tr>
<tr>
<td>The use of selective antibiotic decontamination of the digestive tract compared to the use of live lactobacilli to prevent hospital acquired infections in Intensive Care patients.</td>
<td>Dr. Verbon AZM</td>
<td>Preventie 2</td>
<td>Intramuraal IC patiënten</td>
</tr>
<tr>
<td>The effects and costs of cranberry use to prevent clinical urinary tract infections in nursing home residents.</td>
<td>Prof. dr. Gussekloo LUMC</td>
<td>Doelmatigheids Onderzoek</td>
<td>Verpleeghuis Verpleeghuis bewoners</td>
</tr>
<tr>
<td>Inzicht in de ontstekingsrespons bij galwegobstructie en galwegenontsteking en preoperatieve behandelingsstrategieën</td>
<td>Prof. dr. Gouma AMC</td>
<td>Agiko-stipendia icterische patiënten</td>
<td></td>
</tr>
</tbody>
</table>

## Mathematische modellering

<table>
<thead>
<tr>
<th>Projecttitel</th>
<th>Hoofdaanvrager Organisatie</th>
<th>Programma</th>
<th>Doelgroep</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical epidemiology and evolutionary genetics of antibiotic resistance genes</td>
<td>Prof. dr. Bonten UMCU</td>
<td>Klinische Fellows</td>
<td>Intramuraal</td>
</tr>
<tr>
<td>Prevention of the spread of antibiotic-resistant pathogens in Intensive Care Units by using mathematical modeling, epidemiological surveillance and bacterial genotyping.</td>
<td>Prof. dr. Bonten UMCU</td>
<td>Preventie 1</td>
<td>Intramuraal Zorgverlener</td>
</tr>
<tr>
<td>Combating antibiotic resistance by integrating molecular biology and mathematical modelling</td>
<td>Prof. dr. Bonten UMCU</td>
<td>Vici</td>
<td>Intramuraal</td>
</tr>
</tbody>
</table>
12.5 Recent antimicrobial resistance projects funded under Framework Programme 7

Listed here are the most recent AMR projects funded under framework programme 7. More information is available at: http://ec.europa.eu/research/health/infectious-diseases/antimicrobial-drug-resistance/projectsfp7_en.html.

1. AEROPATH: identification, characterisation and exploitation of novel Gram-negative drug targets
2. AntiPathoGN: identification and validation of novel drug targets in Gram-negative bacteria by global search: a trans-system approach
3. CAREPNEUMO: combating antibiotics resistant Pneumococci by novel strategies based on in vivo and in vitro host-pathogen interactions
4. CONCORD: control of community-acquired MRSA: rationale and development of counteractions
5. DIVINOCELL: exploiting Gram-negative cell division targets in the test tube to obtain antimicrobial compounds
6. HYPERDIFF: the physiological basis of hypervirulence in C.difficile: a prerequisite for effective infection control
7. NABATIVI: novel approaches to bacterial target identification, validation and inhibition
8. PILGRIM: preventing community and nosocomial spread and Infection with MRSA ST 398 - instruments for accelerated control and integrated risk management of AMR
9. PNEUMOPATH: a comprehensive dissection of pneumococcal-host interactions
10. TROCAR: translation research on combating AMR
12.6 Programme committee members

Chair
Dhr. J.M.M. de Gouw          GGD Hollands Midden, Leiden

Co-chair
Prof. dr. J.W.M. van der Meer     Universitair Medisch Centrum St. Radboud, Nijmegen

Members
Prof. dr. M.W. Borgdorff         Academisch Medisch Centrum Amsterdam
Dr. B.W.K. Ganter               World Health Organization, Genève, Zwitserland
Prof. dr. F.M. Haaijer-Ruskamp  Universitair Medisch Centrum Groningen
Prof. dr. A.P. Hardon           Universiteit van Amsterdam
Prof. dr. J.A.P. Heesterbeek    Faculteit Diergeneeskunde Universiteit Utrecht
Dr. M.E.J.L. Hulscher           UMC St. Radboud IQ Healthcare, Nijmegen
Dr. M. Kretzschmar              Universitair Medisch Centrum Utrecht/RIVM, Bilthoven
Mw. R. Lelie – Van der Zande    KNMP Geneesmiddel Informatie Centrum, Den Haag
Mw. A. Timen                    RIVM / LCI, Bilthoven
Prof. dr. C.M.J.E. Vandenbroucke-Grauls VU Medisch Centrum Amsterdam
Prof. dr. Th.J.M. Verheij       Universitair Medisch Centrum Utrecht
Prof. dr. G. Verschraegen       Universitair Ziekenhuis Gent, België
Prof. dr. J.A. Wagenaar         Faculteit Diergeneeskunde Universiteit Utrecht
Prof.dr. B.A.M. van der Zeijst  Nederlands Vaccin Instituut, Bilthoven

Observers
Mw. M. Kraaij-Dirkzwager       Ministerie van VWS directie PG, Den Haag
Dr. Ir. A. Meijering            Ministerie van LNV, Den Haag
Dhr. H. Seeverens              Ministerie van VWS directie GMT, Den Haag
Dr. E. Rijkers                 NWO/WOTRO, Den Haag
### 12.7 Timeline

<table>
<thead>
<tr>
<th>Date/Time</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>18 September 2009</td>
<td>First call opens</td>
</tr>
<tr>
<td>10 November 2009, 15.00</td>
<td>Deadline submission Project ideas</td>
</tr>
<tr>
<td>Mid-January 2010</td>
<td>Meeting Programme Committee</td>
</tr>
<tr>
<td>End January 2010</td>
<td>Committee recommendations to submitters</td>
</tr>
<tr>
<td>23 March 2010, 15.00</td>
<td>Deadline submission Proposals</td>
</tr>
<tr>
<td>End June 2010</td>
<td>Decision, awarding/rejection letters</td>
</tr>
<tr>
<td>End December 2010</td>
<td>Deadline for start of project</td>
</tr>
<tr>
<td>Early 2011</td>
<td>Second call opens</td>
</tr>
<tr>
<td>End 2012</td>
<td>Third call opens</td>
</tr>
</tbody>
</table>

Information on ZonMw’s general time schedule is available on [http://www.zonmw.nl/nl/subsidie/procedure/hoe-lang-duurt-de-procedure/](http://www.zonmw.nl/nl/subsidie/procedure/hoe-lang-duurt-de-procedure/)
12.8 References


(6) Scientific opinion of the panel on biological hazards on a request from the European Food Safety Authority on foodborne antimicrobial resistance as a biological hazard. The EFSA Journal 2008;765:1-87.


(15) Kasteren van MEE. Improving the prescription of antibiotics Radboud University Medical Center, Nijmegen; 2007.


(18) European antibiotic awareness day. ECDC 2009Available from: URL: antibiotic.ecdc.europa.eu/


(22) Signalement Goed gebruik van Geneesmiddelen. ZonMw 2009. Conclusions and recommendations of the expert meeting are available on request. jager@zonmw.nl, telephone 070 3495204