Ministerie van Volksgezondheid,
Welzijn en Sport

> Return address Post Box 20350 2500 EJ The Hague

Dutch House of Representatives

2500 EA The Hague

Visiting address:
Parnassusplein 5
2511 VX The Hague
www.rijksoverheid.nl

Reference
767152-136545-PG

Appendices
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Correspondence should be addressed exclusively to the return address, citing date and reference of this letter.

Date 24 June 2015
Subject Approach to antibiotic resistance

Dear Chair,

Increasing numbers of bacteria are developing resistance to antibiotics. This means that some infections are difficult, sometimes even impossible, to treat. Thus, treatments and operations that are now common may entail a significant additional health risk in the future. Despite the fact the problem is largely 'invisible', antibiotic resistance represents a global threat to public health. Antibiotic-resistant bacteria do not respect international borders. Therefore, international cooperation is a priority when dealing with antibiotic resistance. A great deal remains to be done in order to manage this threat, including in the Netherlands.
The approach to antibiotic resistance we propose in this letter addresses all domains where human health is threatened by antibiotic-resistant bacteria; healthcare, animals, food and environment. We refer to this integrated approach based on a public health perspective as the One Health approach. Specific measures will be taken in each domain. Particular attention is required for innovation and international activities. The main focus within the approach to antibiotic resistance in the Netherlands itself lies in healthcare and animal farming. Additionally, this letter includes a position on the Health Council advisory report 'Antibiotics in hospitals: prophylaxis and antibiotic stewardship'. The reaction to the report 'Institutions in geriatric care still do not take the necessary actions to improve hygiene and infection prevention' by the Healthcare Inspectorate is also included in this letter. Both reports are enclosed. The outlined approach also fulfils intentions as formulated in the letter of 2 July 2013[1].

Tackling antibiotic resistance is an ongoing endeavour. The proposed approach focuses on the period 2015-2019. Part of this approach includes an elaboration of the European Presidency during the first half of 2016. The Ministries of Health, Welfare and Sport and Economic Affairs have both indicated antibiotic resistance is

[1]House of Representatives, 2012-2013, 32620, no. 91

a shared priority.

The letter outlines the overall goals per subsector. Appendix 1 describes concrete actions designed to realise these goals in the coming years.

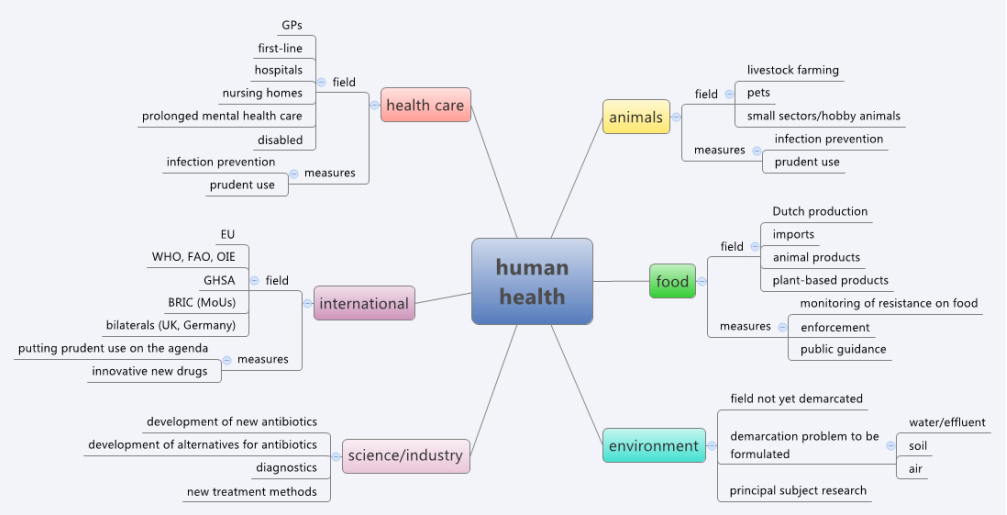

Figure 1: scope of the approach

1. International

Antibiotic resistance is a cross-border problem at global level, affecting both developed and developing nations. However, the mandate for enforcing international measures is limited. We continue to strive to put a One Health approach on the international agenda, and remind health ministers of their coordinating responsibility; they must press for measures in all sectors in the interest of public health. Wherever possible, we enter into further cooperative agreements with various countries. The Netherlands wants to contribute to a safer environment and thus reduce the import of resistance. International cooperation also increases the effectiveness of measures and (research) investments. Besides, Germany is set to place antibiotic resistance on the G7 agenda during a meeting of health ministers in late 2015.

WHO Global Action Plan
The Global Action Plan on antimicrobial resistance was adopted during the annual meeting of the World Health Organization (WHO) in May 2015. Together with a number of member states, the Netherlands has worked hard on the realisation of this plan, among other via the joint Ministerial conference organised in The Hague in June 2014, by the Ministry of Health, Welfare and Sport and the Ministry of Economic Affairs. Good implementation of the WHO Global Action Plan on antimicrobial resistance in the coming years is of great importance. We support the WHO, FAO[2] and OIE[3] in these efforts. In concrete terms, this includes a

[2] Food and Agricultural Organization of the United Nations
[3] World Organisation for Animal Health

specific financial contribution from the Ministry of Health, Welfare and Sport to the WHO, and strategic secondments to the WHO. We are currently discussing a high-level strategic secondment with the WHO.
Additionally, the National Institute for Public Health and the Environment (RIVM) was recently appointed as WHO Collaborating Centre for Antimicrobial Resistance Epidemiology and Surveillance. This means the RIVM provides technical support to WHO member states in creating and strengthening surveillance of resistant bacteria, following the Dutch model. Attention is also given to antibiotic resistance in developing nations via Dutch support for the Global Fund for AIDS, Tuberculosis and Malaria, with a particular focus on multiresistant tuberculosis.

Global Health Security Agenda
The Netherlands, together with a number of like-minded countries, is involved with the Global Health Security Agenda. The United States of America took the initiative to draft this agenda, and asked other countries to help with the implementation. The strategy consists of eleven 'action packages'. The Netherlands is actively involved in the action packages antibiotic resistance and zoonotic diseases. Together with our fellow 'leading countries'[4] in the antibiotic resistance action package, the Netherlands strives to strengthen and improve coordination of technical assistance provided to countries who request it. Naturally, this is done based on demand and in close consultation with the WHO. Additionally, the leading countries develop an approach specifically for countries where combating and preventing antibiotic resistance is still in its infancy. In doing so, we contribute to the implementation of the WHO antimicrobial resistance Global Action Plan and other international guidelines. Via this international partnership, we also motivate our partners to reduce antibiotic resistance in animal farming within their countries. We introduce them to our policies based on the precautionary principle and the practice of reducing antibiotic usage in animal farming in the Netherlands. With regard to the Zoonotic Disease action package of the Global Health Security Agenda, the Netherlands provides technical support to Indonesia for improving the detection and prevention of zoonotic diseases. Appendix 2 presents the current state of affairs of the Dutch approach to zoonotic diseases. The Minister of Health, Welfare and Sport plans to attend the Global Health Security Agenda meeting in South Korea in September of this year in order to present the activities targeting antibiotic resistance and discuss potential next steps that can be taken together.

European Union Presidency
During the first half of next year, the Netherlands will have the presidency of the European Union (EU). Antibiotic resistance is one of the Cabinet's priorities during this presidency. We are of the opinion that at EU level benefits can still be gained from the already announced follow-up to the EU Action Plan against antimicrobial resistance. The current Action Plan was drafted in 2011 and ends in 2016. In March 2015, an agreement was reached with European Commissioner Andriukaitis to present the evaluation of the current Action Plan during a Ministerial conference, for which the Dutch Ministries of Health, Welfare and Sport and Economic Affairs will invite EU ministers of both Agriculture and Health. Such a joint conference is unique, and of major importance with regard to the One Health approach. This evaluation, along with previous Council conclusions on antibiotic resistance drafted during the Danish presidency in 2012, and which follow the

[4] The United Kingdom, Sweden, Germany and Canada

themes of the EU Antimicrobial Action Plan[5], may act as a starting point for a debate towards further agreements. The specific objective is reaching consensus on surveillance of resistant bacteria and antibiotic use in human healthcare, as a basis for developing infection prevention measures and promoting prudent use of antibiotics. Furthermore, we will strive for reduction of the use of critical antibiotics in animals. From a public health perspective, a ban on the use of last resort antibiotics (such as carbapenems) for the treatment of animals will be addressed, with reference to the current legislative process of relevant EU regulations . We will also draw attention to food safety aspects, authorisation of new antibiotics, and gaps in the development of new antibiotics and alternatives for antibiotics. In order to further emphasise the importance of a One Health approach to antibiotic resistance, we will strive to place the outcomes of the conference on both Health Council and Agriculture Council agendas as Council Conclusions. Finally, we will urge the European Commission to initiate a Joint Action between EU member states where key policy developments in the domain of antibiotic resistance may be exchanged.

2. Healthcare

Compared with other countries, the Netherlands performs relatively well where the prevention of infections and prudent use of antibiotics are concerned[6]. However, the reports by the Dutch Healthcare Inspectorate published in late 2013 on hospitals and nursing homes show that there is room and a need for improvement. The recent report on hygiene and infection prevention in nursing homes (appendix 3) leads to the conclusion that greater efforts are required on behalf of long-term care institutions. This additional effort will focus on developing better policies and embedding them more fully in institutional procedures. Additionally, nursing homes and hospitals will participate in regional surveillance, as recommended by the Health Council (appendix 4) and the regional containment of resistance. This will lead to greater transparency and provide additional incentives to achieve higher quality of care.

Regional cooperative networks
Cooperation between institutions and between various healthcare sectors is currently insufficiently organised to ensure antibiotic resistance can be managed in a future-proof manner. Patients pass through the entire (regional) healthcare chain. Healthcare providers and health facilities, such as hospitals, nursing homes, municipal health services, rehabilitation clinics, GPs and home care institutions, will need to work together in a single network. It must be clear who is responsible for what. This is the only way to ensure the spread of infectious diseases and antibiotic resistance is controlled in an effective manner. There are some good examples in the Netherlands already, such as the *Regionaal Preventienetwerk Noord-Nederland* (Regional Prevention Network for the North of the Netherlands). A regional network of laboratories is active in the North of the Netherlands, targeting the spread of antibiotic resistance. Based on its own scientific research, the Medical Microbiology department of the UMCG has created a regional cooperative network, together with CERTE-LvI, IZORE Friesland, Isala Clinics in Zwolle, and Labmicta Twente/Achterhoek. The core activity is the monthly

[5] 'the impact of AMR in the human health sector and in the veterinary sector – a one health perspective'
[6] http://www.efsa.europa.eu/en/efsajournal/doc/4006.pdf

'REgional Microbiological Infectiological Symposium' (REMIS), where members of all relevant professions can meet for extra training, to exchange and analyse current (typing) data, and coordinate joint activities (such as screening). The REMIS is also intended to highlight the appearance of unique microorganisms in one or more institutions within the region. In early 2015, this cooperative network was further strengthened by a regional declaration of intent in order to organise interdisciplinary prevention, diagnosis and treatment recommendations on a regional level in the future.

Surveillance and monitoring
Efforts are also necessary in the domain of surveillance. Effective control of infectious diseases requires timely and adequate insight into who becomes ill where, when and why, and how the underlying infections spread. Central coordination is crucial to bring together the current fragmentation. This also involves the (financial) assessment of public interests on the one hand, and the interests of individual patients/carriers and health facilities on the other. The balance between these interests will be given special attention.

Multi-annual healthcare agenda
Actors in the healthcare sector recognise and confirm the problems and urgency, and have confirmed their willingness to work on finding solutions that encompass the entire scope of the healthcare system. This has resulted in a joint mission and six goals[7].

'*Avoidable harm and mortality among patients due to infections caused by resistant bacteria must be prevented wherever possible. To this end, the further development and spread of (multi)resistance must be managed as much as possible, in order to ensure that effective treatment of infections with antibiotics remains possible in future.*'

Actors agree to the following goals:
1. A significant further reduction in the emergence and spread of multiresistant bacteria in healthcare becomes visible during the next five years. Developments abroad (e.g. Germany and Belgium) will serve as a frame of reference. A relevant benchmark will be developed to measure the further reduction[8]. This applies to both carriers of and infections with resistant bacteria.
2. Early detection of and swift response to resistant bacteria and other infectious threats ensure that the number of carriers[9] of resistant bacteria and the number of infections and deaths due to antibiotic resistance in the Netherlands will remain at the current level or decrease (significantly).
3. During the next five years, international cooperation with other EU countries regarding antibiotic resistance will be promoted, in order to realise an infrastructure that allows for the joint management of reducing the development and spread of antibiotic resistance.
4. The number of avoidable healthcare-associated infections [10] will be reduced by 50% in five years, compared with a baseline defined by the relevant actors.

[7] All parties involved have indicated they agree with the formulated mission and goals, although a number of parties can only formally approve the implementation of agreements after the summer.
[8] http://www.efsa.europa.eu/en/efsajournal/doc/4006.pdf
[9] Carriers: not everyone carrying a resistant bacteria will develop an infection.
[10] A healthcare-associated infection (formerly: hospital infection) is an infection that

Differences between healthcare domains and practice variation within each domain will be taken into account.

5. The possibilities for effective treatment of patients with infections with resistant bacteria will not reduce any further during the next five years.
6. During the next five years, the objective is to achieve a reduction of at least 50% in the use of incorrectly prescribed antibiotics across the entire healthcare chain, relative to a baseline determined with stakeholders. Differences between healthcare domains and practice variation within one domain will be taken into account. Further agreements between the stakeholders will be founded on the baseline assessment. It is important to consider agreements about prescription behaviour within the context of quality of care; both over-treatment with antibiotics and under-treatment will be taken into consideration.

These goals have been used as a basis for a multi-annual agenda. The agreements made with the healthcare sector and the multi-annual agenda are enclosed with this letter as appendix 5 (a and b). The measures are in line with Health Council recommendations on antibiotic use in hospitals with regard to antibiotic stewardship, monitoring of prophylactic use and surveillance. Additionally, there will be a strong focus on research into new antibiotics, new treatments and innovative(medical) technology. A communication strategy targeted towards professionals and the general public will be developed, aimed at raising awareness on the urgency of the problem , and personal responsibility. We express our appreciation for the fact that all involved parties recognise that antibiotic resistance is a shared problem, and that a joint approach is required. After all, the chain is only as strong as its weakest link. Naturally, we will monitor the implementation of the multi-annual agenda and inform Parliament on its progress at regular intervals.

3. Animals

Use of antibiotics in animals, like all use of these medicines, entails a risk of resistance developing in bacteria. Additionally, animals are a potential reservoir from which resistant bacteria can multiply and spread. This is a threat to public health and veterinary health. Therefore, the goal is reduction and prudent use of antibiotics in animal farming in order to limit the development of resistance where possible. Over the past years, the four major animal farming sectors and veterinarians have made major efforts towards this goal.

Less and prudent use in animal farming and other animal species
In the letter of 27 May 2015 (EZ/DGAN-DAD/15069143), we informed you of the outcomes of the SDa (the Netherlands Veterinary Medicines Authority)report on antibiotic use in animal farming in 2014. The SDa notes that veterinary antibiotic use dropped by 4% in 2014 across the four major animal farming sectors, following a period of major drops. This means the reduction of antibiotic use has flattened. This was expected, as the SDa concluded. In 2014, the poultry sector

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develops during a hospital stay or treatment in a care institution (hospital, nursing home, independent treatment centre) [source:*http://www.nationaalkompas.nl/gezondheid-en-ziekte/ziekten-en-aandoeningen/infectieziekten-en-parasitaire-ziekten/zorginfecties/wat-zijn-zorginfecties-en-welke-factoren-beinvloeden-de-kans-op-zorginfecties/]*

displayed a rise in use after years of swift reduction, while the pig and veal calf farming sectors displayed a slight reduction. The cattle farming sector achieved a significant reduction in 2014. For the specific developments per sector and the measures taken by these sectors to achieve further reductions, we refer you to the letter to Parliament of the 27th of May 2015.

The total reduction compared with 2009 is 58.1%. The study also shows that there are significant differences between sectors and between veterinarians. The use of antibiotics critical to public health (3rd and 4th generation cephalosporins and fluoroquinolones) has been reduced to almost zero in the major animal farming sectors - a gratifying result. Resistance levels of bacteria in livestock have also dropped in recent years. We greatly appreciate the results achieved by the sectors and veterinarians to date. However, we consider the flattening of the decrease a cause for serious concern. We are not there yet, and additional efforts will be required for further reductions. Our current goal focuses on a 70% reduction compared with 2009. The sectors and veterinarians will need to do everything in their power to further reduce antibiotic use. In order to achieve a further reduction, effort is needed specifically on:

- Additional measures by sectors/veterinarians and strong continuation of implementation of the current policy. The large animal farming sectors face the challenge of stimulating farmers and veterinarians in the 'action area' (red) and the 'warning area' (orange) to shift towards the 'target area' (green) of restrained and prudent antibiotic use. The sectors and veterinarians have already prepared additional measures that will be executed in 2015.
- Prudent and restricted use in other animal sectors (pets, horses, rabbits, etc.) along with reduction of critical antibiotic use in these sectors to this end. We will develop an approach in 2015.
- Continuation of more stringent NVWA (the Netherlands Food and Consumer Product Safety Authority) inspections and enforcement of restricted antibiotic use in animal farming and identification and control of illegal activities.
- Improvement of general animal health in order to achieve extremely restricted antibiotic use. This is a crucial challenge for actors in the chain, sectors and individual animal farmers, in consultation with their veterinarians. It is important that restricted and prudent antibiotic use is linked to the innovation and sustainability agendas of all the chains affected.

Europe

In Europe, we strive for reduction of the use of critical antibiotics in animals. In the context of a recently proposed European Regulation on veterinary medicines, we pursue measures that contribute to a major reduction of the use of these substances in Europe. For example, we propose mandatory susceptibility testing prior to use of these medicines to be included in this new Regulation. Additionally, we aim for a general ban on the use of last resort antibiotics (such as carbapenems) in animals in this Regulation. These last resort antibiotics are not authorised for veterinary use. . Use of these medicines in food producing animals is not permitted according to current regulations. Via the so-called cascade regulation[11], however, these last resort antibiotics can still be used in the EU in animals which are not used for food production, such as pets. Measures have already been put into place to combat use in pets in the Netherlands. Based on

[11] Cascade regulation: the European regulation that allows veterinarians to apply medicines not authorised for the animal species or disease in question under exceptional circumstances.

professional guidelines for veterinarians ('formularia'), these last resort antibiotics may not be used for dogs and cats in the Netherlands.

Also, in 2015 we will work together with stakeholders to develop a new policy to prevent the introduction and spread of carbapenem-resistance in animal farming and in the food chain. This policy will be presented to Parliament at the end of 2015.

Evaluation and policy 2016-2020
We will use 2015 to consult with veterinary and human medicine experts, the SDa, the animal farming sector and veterinarians, on a new policy to be implemented from 2016 onward. This policy will focus on the further reduction of the risks of the development and spread of resistance in animal farming to public health and animal health. The approach will be formulated per sector, with specific goals per animal species where possible. The goal is an animal farming sector where the health of the animals in the entire chain is the norm, and disease and antibiotic therapy the exception. In order to achieve this, it is crucial that all partners in the entire chain focus on the prevention of animal diseases.
We use the following elements to formulate follow-up policy:

- The Health Council will issue an update of its 2011 advisory report regarding the public health risks of antibiotic use in animal farming late 2015.
- The SDa will issue an advisory report late 2015 regarding a benchmark system related to resistance levels, and the possibilities for developing more animal-specific (reduction) targets rather than the current, generic targets.
- The Council on Animal Affairs will publish a position paper late 2015 on the consequences of the reduction policy for animal welfare and health, and advise on prudent and restricted use of antibiotics while maintaining animal welfare and animal health.
- While developing a new policy, attention will also be given to the effect of antibiotic use in animals on the environment (see paragraph 5 on the environment in this letter).
- The knowledge agenda on ESBL in the food chain will be completed in the summer of 2015. This will allow greater focus and prioritisation of future research efforts. This may further shape policy on managing ESBL-producing bacteria.

We will inform the Parliament of the follow-up policies in early 2016.

4. Food safety

An effective approach to antibiotic resistance and the food chain requires greater knowledge about the transmission route, and the specific attribution of food to antibiotic resistance. Therefore, we focus strongly on continued monitoring and research. Subsequently, the reduction of transmission of resistant bacteria via food can be pursued at the international level.

Research
Both nationally and internationally a great deal of research is being conducted into various transmission routes for antibiotic resistance, including transmission via food. More knowledge is required in order to create a focussed approach.

Monitoring, standards and enforcement
From 2002 onwards, the Netherlands has monitored the occurrence of antibiotic

resistance in animals and food. From 2014, all European member states are monitoring for resistant bacteria in animals and food thanks to mandatory European regulations. As of 2014, surveillance of the potential introduction of highly undesirable carbapenem-resistance has become [12]part of this monitoring. For example, imported farmed fish is screened for the presence of resistant bacteria. The Netherlands is a leading country within the EU in this area, and will urge further development of standards and monitoring on a European but also global scale. In the Netherlands, a number of activities will also start in order to reduce exposure of consumers to resistant bacteria via food.

Raising public awareness
Consumers can also prevent exposure to resistant bacteria by preparing food in a hygienic manner. The Netherlands Nutrition Centre informs consumers about general hygiene guidelines that can contribute to general food safety. For example, in October 2014, a campaign aimed at raising public awareness- 'Ziekmakers zie je niet' ('You can't see what makes you ill') was commissioned by the Ministry of Health, Welfare and Sport. A follow-up campaign will be launched in the summer of 2015. In addition to taking action aimed at raising public awareness, we expect to receive the outcome of the study on the effectiveness of the current warning label on fresh poultry shortly. Depending on the results of this study, we will consider expanding the current warning label on poultry to other high-risk products.

5. Environment

Knowledge about the development of, the occurrence of and the spread of antibiotic resistance in people and animals, but also in the environment (soil, water and air) is crucial to controlling antibiotic resistance. Very large numbers of bacteria enter the environment each day via humans and animals. If a minority is resistant, this still represents a lot of bacteria that humans may be exposed to. Additionally, (traces of) antibiotics also end up in the environment. How these (traces of) antibiotics and these resistant bacteria behave in the environment, how dissemination occurs, and what the consequences are for public health remains unknown.

Knowledge outline and policy recommendations
The Netherlands Organisation for Health Research and Development (ZonMw) and the National Institute for Public Health and the Environment (RIVM) have drafted a knowledge outline[13] and policy recommendations[14] regarding antibiotic resistance in the environment, without considering the role of (traces of) antibiotics in the environment. This revealed that a great deal of national and international research has been conducted, but that results are difficult to compare due to the use of different criteria and quality requirements. Other notable findings include:

- The presence of resistant bacteria in the environment differs significantly per country.

[12] Based on the EFSA advisory report: 'Scientific Opinion on Carbapenem resistance in food animal ecosystems.' December, 2013
[13] Knowledge outline 'Role of the environment in the transmission of antibiotic resistance to humans', ZonMw, 2014
[14] Policy recommendations: The role of the environment in the transmission of antibiotic resistance to human*n*s, RIVM, 2015

- No research encompassing the entire chain from source, extent of contamination, carriers and risks for humans has been performed.
- There is insufficient information about the attribution of various sources to resistance in the environment, the extent to which specific bacteria occur in the environment, and the resulting risks.

Action plan for effective management measures
Despite these uncertainties, the research by ZonMw and the recommendations by the RIVM show that the environment does play a role in the transmission of antibiotic resistance. This outcome provides ample reason to initiate a number of activities.

1. We will ask the RIVM to draft an action plan for gaining better insight into the situation in the Netherlands. Where necessary, the RIVM will involve other actors (e.g. veterinary institutions/experts). This action plan must result in an advisory report on the most effective management measures by mid 2016. At the very least, the implementation of the action plan must encompass measurement of the occurrence of resistant bacteria and the presence of (traces of) antibiotics in the environment. To this end, measurements will be performed in waste water from health facilities and residential areas, in waste water treatment plants and in manure, among other places. The research will begin soon. Besides, the Ministry of Economic Affairs has commissioned research into the presence of antibiotic residues in manure. The studies will be harmonised.
2. Additionally, antibiotic resistance will be included in a number ofinitiatives, such as the Green Deal sustainable operations in healthcare[15] and in the new water quality policy.

6. Innovation

Innovation is an essential precondition for effective control of antibiotic resistance. This pertains not only to the development of new antibiotics, but also to improvements in infection prevention, prevention of spread of resistant bacteria, improved application and much faster diagnoses, and alternative treatments focused on reducing the use of antibiotics.

Product innovation
The urgent need to develop new and improved antibiotics is felt broadly by Dutch stakeholders in the sector, such as universities, knowledge institutes, pharmaceutical companies and university hospitals, and all actors are willing to contribute to a solution.
The Netherlands has a solid reputation in research into (controlling) infectious diseases, and has a solid infrastructure to stimulate innovation. The cooperation between various research groups and the Dutch research climate is not ideal, however, and must be strengthened. The current business model for the development of new antibiotics is characterised by the fact that anticipated returns on investment are quite insufficient. Companies that invest a great deal of

[15] Green Deals offer companies, private individuals and organisations a low threshold way to work on green growth together with the government. Grassroots initiatives are the foundation of this process. Where these initiatives run into obstacles that can be addressed at the national level according to the project initiators, the Cabinet wants to help remove said obstacles in order to facilitate and accelerate these initiatives. In a Green Deal, parties put such concrete agreements in writing.

money in research and development and are successful in doing so, also know that these new products are prescribed as little as possible, and are preferably not used. These medicines need to be developed to be used as last resort antibiotics, and held back whenever possible. This means that use will be minimal in an ideal world. As a result, the possibilities for investment in the development of these medicinal products are practically absent.
Finally, fundamental and translational [16] research into new antibiotics and alternatives requires more attention. Clinical research is considered to be expensive and time-consuming.

Based on these signs, we define the following approach:

1. We will strengthen cooperation between research institutions and companies based on a national knowledge agenda, to be defined jointly, which will be used to guide activities. The strengthened research infrastructure will result in a network where knowledge is shared, and fundamental, translational and clinical research come together in order to ensure optimal coordination within the innovation chain. Where possible, research results are shared in public-private partnerships in order to promote further development. The concrete interests of knowledge institutions and the business sector will be examined in advance. To implement the strengthening of the research infrastructure we will line up with existing initiatives, research institutions and centres of expertise and the so-called Dutch top sectors Life Science and Health (LSH), Chemistry and Agro for the further development of research infrastructure.
2. We support and cooperate in international initiatives designed to develop new business models. An existing example is the project 'DRIVE-AB', which is funded via the European Innovative Medicines Initiative and is also part of the WHO Global Action Plan on antimicrobial resistance. Together with other countries, the WHO and NGOs, we examine whether developments and good use of new medicines can be stimulated via a public-private initiative, as is currently the case for poverty-related diseases. The G7, under German leadership, seems to have expressed its interest.
3. We identify the main bottlenecks in the development and marketing authorisation process, and do everything possible to accelerate clinical research with and the authorisation process for new antibiotics. This is an international endeavour undertaken in cooperation with the Dutch Medicines Evaluation Board, the National Institute for Public Health and the Environment and the European Medicines Agency.
4. We support the development of international fundamental scientific knowledge by commissioning a new assignment to The Netherlands Organisation for Health Research and Development (ZonMW) and by supporting permanent participation in the European Joint Programming Initiative on antimicrobial resistance. This programme strives for better cooperation between EU member states (but also partner nations such as Canada) in the field of research in order to harmonise national research programmes and jointly initiate and fund expensive and complex research.

With this approach, we hope to underline the importance of developing new medicines as one part of the integrated approach. We note that we do not expect this will result in new products in the short term. It will take some time for results from fundamental research to result in a medicine that can be applied in patients. However, considering the scope of the problem, doing nothing is not an option.

[16] Translating insights from fundamental research to clinical applications.

Innovation aimed at the prevention of infections and their spread and alternatives to antibiotics
In addition to the development of new medicines, there are also gains to be achieved by new initiatives regarding alternative treatments, infection prevention and countering spread.
Scientifically sound alternative treatments for bacterial infections may prove to be a valuable alternative to therapy with antibiotics. There are a number of promising products on the market, for example for treating urinary tract infections or acne. These products must now prove their worth in practice. It is now up to professional groups, The National Health Care Institute (Zorginstituut Nederland) and insurers to determine the added value of these products and give them a place within current guidelines and health insurance packages.
In curative and long-term care, we see countless examples of innovation in the domain of infection prevention and prevention of spread. Examples include urinary catheters with antimicrobial coatings, an infection prevention outpatient clinic, infection prevention apps, and mobile inflatable airlocks for isolation rooms, but also very simply solutions such as a mirror in an airlock to an isolation room so people can check whether their mask is fitted properly. Some hospitals also deploy innovative methods for cleaning hospital waste water of trace antibiotics and (resistant) bacteria. The opportunities and obstacles facing broad implementation of such innovations in healthcare are as yet unclear. A new ZonMW antibiotic resistance programme will have to remedy this. The 'quality programme in long-term care' and the 'experimental article' (a temporary article intended to evaluate the results of implementing new policy) will promote the development of innovations.

7. Communication

Multi-annual communication strategy
The issue of antibiotics affects many groups and stakeholders that influence each other. For example, increased awareness, knowledge and changes in the behaviour of the general public can also affect the behaviours of professionals such as GPs or nurses. In turn, they influence the attitude of administrators. The reverse is also true: administrators aim to guide professional behaviour regarding for example guideline adherence. Professionals influence the behaviour of the general public by discussing (not) prescribing antibiotics and educating the public about the use of antibiotics and preventive measures designed to reduce bacterial infections.

Coherent communication initiatives in the context of the One Health approach to antibiotic resistance are crucial throughout the chain of public-professionals-administrators. A multi-annual communication strategy will be developed targeting all: the public, professionals and administrators. This strategy includes:

- Increasing public awareness of the problem and increasing knowledge about how antibiotics work and should be used. A national campaign must raise public awareness and give people more knowledge on which to base their own choices. The campaign will provide simple, concrete tips for prevention. The communication efforts will use existing instruments and channels wherever possible, and new tools will be developed as needed. Additionally, communication will be carried out by parties close to the public, such as GPs and pharmacists, supported by the necessary campaign materials.

- For *professionals*, the strategy consists of sharing knowledge and stimulating new developments. Additionally, there will be more focus on reminding professionals of the sense of urgency, placing it higher on the agenda. Suggested courses of action will also be offered within the professional field, for example in the domain of hygiene.
- Among *administrators*, it comes to the further development and activation of existing networks. Solutions for this complex problem can only arise from cooperation between all actors. As is the case for professionals, placing the topic on the agenda and increasing the sense of urgency is part of communication with administrators.

Based on the results achieved in 2015, a multi-annual approach will be developed for communication initiatives starting 2016. The multi-annual communication strategy has the following overall goals:

- Increase awareness among the general public and professionals, and provide knowledge about the use and effect of antibiotics. Themes include finishing a treatment, not prescribing antibiotics for viral infections, and only using antibiotics if the GP deems it necessary and there are no alternatives.
- Providing concrete advice on the prevention of bacterial infections. Themes include food safety, hygiene, transmission of (resistant) bacteria via pets and the importance of following instructions about the use of antibiotics and hygiene guidelines.
- Using accessible information and a structure for raising awareness via easily accessible ways of communication and existing as well as new websites and educational forums.

Differentiation by audience/theme and phased introduction
The general public, professionals and administrators are the main target group in the communication strategy. The general public can be divided into, for example, families, youth, the elderly, or more specifically, patients, pet owners, carriers of resistant bacteria, international travellers, etcetera. Professionals include GPs, medical specialists, nurses and carers. Administrators operate in various (healthcare) sectors with specific priorities and funding. These include hospitals, long-term care facilities, rehabilitation centres or home care. The themes related to the issue of antibiotics have a different impact or meaning for each of these audiences. As regards the messages, channels and facilities, as well as timing, the communication strategy will be tailored to the specific situation of these target groups.

Communication by the Ministry of Health, Welfare and Sport and healthcare actors
The Ministry of Health, Welfare and Sport and all healthcare actors will need to meet their responsibility and fulfil their roles as initiator, communicator or organiser of activities that are part of the harmonised communication strategy. Who do the defined target groups listen to, and what available communication tools suit their media preferences. This not only requires coordination between parties regarding the strategy, but also firm agreements about the organisation of activities and an effective, coherent effort by all involved actors, including the Ministry of Health, Welfare and Sport, the National Institute for Public Health and the Environment RIVM, the Dutch Healthcare Inspectorate, the Netherlands Nutrition Centre, the Netherlands Food and Consumer Product Safety Authority NVWA, the Dutch Patients and Consumers Federation NPCF and healthcare (umbrella) organisations.

Concrete activities for 2015

In the fall we will launch an easily accessible general public awareness campaign. As part of this effort, we will distribute a special issue of the comic Luke and Lucy, Auntie Biotica, in GP waiting rooms as quickly as possible after the summer holidays. This special issue is an initiative of the Belgian Committee for the Coordination of Antimicrobial Policy (BAPCOC) and addresses appropriate use of antibiotics via accessible information for the general public. The comic is included in appendix 6. The comic is also available via the website www.gebruikantibioticacorrect.be . Additionally, the most important information about the effect and the use of antibiotics, prevention measures and guidelines will be clearly presented in a web portal. The national government's website already contains information, for example an infographic to picture the approach in a simple image and web links to twe short clips developed by the RIVM which explain to the general public how antibiotic resistance develops and spreads.[17]
The follow-up to the public awareness campaign by the Netherlands Nutrition Centre ('Ziekmakers zie je niet', 'You can't see what makes you ill'), which focuses on raising awareness, improving knowledge and providing concrete recommendations for both kitchen hygiene and preparing and storing food in order to reduce pathogens, is scheduled for this summer.
Two communication activities will be deployed at the international level:

1. During the previously mentioned meeting of the Global Health Security Agenda in South Korea in September 2015.
2. In preparation of the European Antibiotic Awareness day in November 2015.

Next steps from 2016 onwards

The principles underlying a coherent communication strategy will be elaborated further later this year. In addition to specific activities targeting the general public in the broadest sense, the strategy targeting professionals and administrators will be realised in cooperation with healthcare actors.

[17] http://www.rijksoverheid.nl/onderwerpen/antibioticaresistentie

Conclusion

A great deal is being asked of all involved parties to ensure that this approach is successful. This is necessary - the time has come for all parties to commit. We are glad to be able to note that all actors now recognise the urgency of the situation and have expressed their intention to assume their responsibility in this domain. We will regularly inform Parliament of the progress of the approach to antibiotic resistance. We propose to send an initial progress report in late December 2015.

Sincerely,

The Minister of Health, Welfare and Sport,

E. I. Schippers

the Secretary of State for Health, Welfare and Sport,

M.J. van Rijn

The Secretary of State for Economic affairs,

A.M. Dijksma

The Secretary of State for Infrastructure and the Environment,

W.J. Mansveld