ANTIMICROBIAL RESISTANCE IN THE NETHERLANDS
An Analysis of the 2015 National Action Plan and Recommendations for the Future
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BACKGROUND

Antimicrobial resistance (AMR) occurs when microorganisms, including bacteria, viruses, fungi and parasites, become able to adapt and grow in the presence of medications that once impacted them. The European Centre for Disease Prevention and Control (ECDC) reported that resistant bacteria infect almost two million people in the European Union (EU) yearly, leading to 30,000 annual deaths. While AMR has been recognised as one of the top threats to global health, AMR rates continue to increase.

In 2015, the World Health Organization (WHO) developed a Global Action Plan (GAP) on AMR. This action plan underscores the need for an effective One Health approach involving coordination among international sectors and actors across different domains and areas of intervention. However, recent reviews highlight that the majority of national AMR strategies are underfinanced and/or do not sufficiently align with the GAP goals and guidelines.

The Netherlands’ most recent National Action Plan (NAP) was developed in 2015. This policy brief reviews the content of that document to identify gaps and provide recommendations for future adaptations.

METHODS

To assess the NAP, a modified assessment tool developed by the European Commission in the Overview report: Member States’ One Health National Action Plans against Antimicrobial Resistance was used. This tool takes into account the WHO/Food and Agriculture Organization/World Organization for Animal Health manual for developing NAPs, the Tripartite survey, and the ECDC assessment tool. Using the tool, a qualitative analysis was carried out in which the presence or absence of an indicator was determined. If present, the quality of the indicator was assessed using the SMART (specific, measurable, achievable, relevant, time-bound) criteria. A colour scale was developed to better understand the NAP’s compliance with the assessment tool: red when the item was absent in the NAP, orange when it was mentioned but of inferior quality, and green when the item was included and of considerable quality.

RESULTS

NAP General Structure

The Netherlands’ NAP was published in 2015 for the 2015-2019 period and has not been updated since. The NAP takes the form of a letter from the then Minister of Health, Welfare and Sport to Parliament. The NAP covers six sectors (international, healthcare, animals, food, environment, and science/industry) that are focussed on human health (see Figure 1). An annex further details the concrete actions to be undertaken per sector.
National Strategy and Action Plan

The NAP follows a “One Health” perspective, is in alignment with the objectives and principles of the WHO GAP on AMR and based on an evidence-based situational analysis. Primary focus of the NAP is on human and animal health, and less so on environmental aspects. Goals and strategic objectives are clearly defined, and while timelines and performance indicators to evaluate progress have been included, they are not very detailed, with responsibilities and general accountability remaining vague. Further, while the NAP was endorsed by Ministers and State Secretaries and adopted as government policy, the plan did not include an estimate of resources needed for multi-year budgetary provisions. On outbreak preparedness and response planning, the NAP plans for active monitoring of antimicrobial stewardship (AMS), prescribing behaviour and policy, as well as development of guidelines regarding outbreak management in nursing homes. However, plans for the management of outbreaks within hospitals and the wider community are not specified within the NAP.

<table>
<thead>
<tr>
<th>1. National strategy and action plan</th>
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<td>1.3.1 Clearly outlined activities and interventions</td>
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<td>1.3.2 Linked to other national action plans on related topics (e.g., healthcare-associated infections/Infection Prevention and Control (IPC), EU-harmonised AMR monitoring in certain animals and foodstuffs) or specific disease areas (e.g., tuberculosis, HIV, STIs)</td>
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### 1.4 Monitoring and evaluation of NAP

1.4.1 Performance indicators
1.4.2 Clearly outlined targets and timelines
1.4.3 Periodic reviews of progress and impact

### 1.5 Preparedness/response planning for AMR

1.5.1 Preparedness and response planning for outbreaks of highly resistant pathogens
1.5.2 Strategy to ensure availability of new and existing antimicrobial agents, including narrow spectrum antimicrobials
1.5.3 Policies/enforcement to address counterfeit products/illegal online sales

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**Intersectoral Collaboration Mechanism**

It is not easy to make sense of the intersectoral collaboration mechanism (ICM) as set out in the NAP. While it is clear that interdisciplinary collaboration occurs, no specific mechanism or stakeholders are mentioned specifically. The annex to the letter does mention multiple government agencies, but it lacks details in terms of interactions or hierarchies.

#### 2. Intersectoral Coordination Mechanism (ICM)

**2.1 Composition of ICM**

2.1.1 Inter-sectoral composition of the ICM
2.1.2 High-level chairpersons from the above sectors
2.1.3 Clearly defined roles, responsibility and accountability
2.1.4 Inclusion of relevant stakeholders (government, industry, professional societies, patient representatives, relevant organisations)
2.1.5 Inclusion of relevant expertise (infectious diseases), epidemiology, IPC, microbiology, pharmacology, surveillance, environment, communications).

**2.2 Regular meetings of ICM**

2.2.1 Meetings of the ICM

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**Awareness and Understanding of AMR**

The NAP describes the development and dissemination of educational information materials and resources from a One Health perspective for the general public and professionals. The NAP specifically mentions a campaign on hygiene measures for preparation and storing of food. However, information on training and professional education is limited and does not specify the type of educational focus points per different professional group. Veterinarians are mentioned as being in need of improved knowledge on AMR via continuing education and peer review but there are no clear indicators on how to achieve that.
3. Awareness and understanding of AMR

3.1 Public awareness-raising activities and understanding of AMR risks response in:

| 3.1.1 Human Health (general public awareness campaigns and campaigns dedicated to specific target groups) |
| 3.1.2 Animal health (specific public awareness campaigns targeting keepers of animals) |
| 3.1.3 Food safety (specific public awareness campaigns concerning the food safety aspects of AMR) |
| 3.1.4 Environment sectors (specific public awareness campaigns concerning the environmental aspects of AMR) |
| 3.1.5 Collaborative communication activities including activities conducted with a One-Health approach |

3.2 Existence of training and professional education on AMR

| 3.2.1 Training and professional education in human health sector |
| 3.2.2 Training and professional education in veterinary sector |
| 3.2.3 Training and professional education in farming sector (animal and plant) |
| 3.2.4 Training and professional education in food safety sector |
| 3.2.5 Training and professional education in environmental sector |

National Monitoring and Surveillance of Antimicrobials in Humans, Animals, and Plant Production

National monitoring systems for the consumption and rational use of antimicrobials in human health and intended for use in animals exist. Data on antibiotic resistance is sent to the European Antimicrobial Resistance Surveillance Network (EARS-Net). However, even though it is known these national monitoring systems exist, little detail is provided. The annex does mention that in all healthcare networks, uniform and reproducible oversight of antibiotic use in relation to the disease, and the status of infection prevention should be ensured. Very limited information is included on the monitoring within animals or plant production.

4. Monitoring and surveillance

4.1 National monitoring system for consumption and rational use of antimicrobials in human health

| 4.1.1 Data collection |
| 4.1.2 Existence of a national monitoring strategy for antimicrobial sales or consumption |
| 4.1.3 Communication of relevant data (rates and trends) to policy/decision makers |
| 4.1.4 Identification of the national trends of use of antimicrobials and major gaps in knowledge on the patterns of use of antimicrobials on national level |

4.2 National monitoring system for antimicrobials intended to be used in animals (sales/use)

| 4.2.1 National legal framework (existing prior to Regulation (EU) 2019/6 becoming applicable) for collection of data on SALES of antimicrobials in animals |
| 4.2.2 National legal framework (existing prior to Regulation (EU) 2019/6 becoming applicable) for collection of data on USE of antimicrobials per animal species |
National Monitoring and Surveillance of AMR in Humans, Animals, and Food of Animal Origin

The NAP includes goals for the Dutch EU Presidency of 2016, as well as many international commitments regarding AMR surveillance, such as countries receiving information on and assistance with surveillance through the National Institute for Public Health and the Environment (RIVM) (appointed as WHO Collaborating Centre for Antimicrobial Resistance Epidemiology and Surveillance); improving surveillance through representation; and the active contribution of the RIVM in various international networks on surveillance of AMR and healthcare-acquired infections. The reference to the Dutch EU Presidency highlights the need for an updated plan; the Dutch EU Presidency was seven years ago. The NAP also includes some specific national actions on surveillance, including that every healthcare facility has a protocol for surveillance of multi-drug resistance, and that AMR-related data should be accessible to all stakeholders. The NAP also wants to ensure involvement of all relevant health stakeholders in the governance of the surveillance system. The NAP does not include information on surveillance of AMR in animals and food of animal origin.

4. Monitoring and surveillance (continued) NL

4.4 National surveillance system for AMR in humans

4.4.1 Existence of a national AMR surveillance plan

4.4.2 Existence of a national reference laboratory/ general coordination of the network of national laboratories

4.4.3 Existence of national body with the ability to systematically gather, and analyse data and trends

4.4.4 Communication of relevant data (prevalence and trends) to policy/decision makers

4.4.5 Identification of major knowledge gaps on AMR in human health sector

4.5 National surveillance system for AMR in animals and food of animal origin

4.5.1 Existence of a national monitoring system (EU legislation)

4.5.2 Existence of voluntary and additional national AMR surveillance plan for pathogens and food/animal combinations not included under the EU harmonised monitoring

4.5.3 Communication of relevant data (prevalence and trends) to policy/decision makers

4.5.4 Identification of major gaps in knowledge on AMR in animal and food of animal origin sector
National Monitoring and Surveillance of AMR in Plants and Food of Plant Origin, and the Environment

Plant health is not mentioned in the NAP, hence neither are surveillance plans on plants and food of plant origin. The environment was also limitedly described in the NAP. All information related to the environment included in the NAP is reviewed in this section. The NAP does not cover standardised approaches or segmented surveillance systems for data collection on AMR in the environment. It also makes no mention of a national network of laboratories for testing, nor on communication of data on prevalence and trends. The NAP does plan to pay more attention to the environment by also including the effect of antibiotic use in animal health on the environment when developing new policies. The main focus of the NAP with regards to the environment is on identifying major gaps in knowledge on AMR in the environment. The NAP proposes the development of an action plan by the RIVM to gain better insight into AMR spread through the environment in the Netherlands. The plan should lead to a proposal on mitigation measures, including, at least, AMR wastewater measurements. However, the NAP does not mention whether wastewater measurements will become an integrated component of surveillance, or if it is only for the development of the action plan. AMR will also be included in a number of initiatives, such as the “Green Deal Sustainable Operations in Healthcare” and in the new water quality policy.

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<th>4. Monitoring and surveillance (continued)</th>
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<td>4.7 National surveillance system for AMR in animals and food of animal origin</td>
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<td>4.7.4 Identification of major gaps in knowledge on AMR in environmental sector</td>
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<td>4.7.5 Communication of relevant data (prevalence and trends)</td>
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Infection Prevention and Control in Human Health and Animals

On IPC, the NAP gives priority to ensuring that all hospitals and nursing homes have active IPC policies, and that any guidelines on hygiene and infection prevention or careful antibiotic use and resistant bacteria are provided through patient information. However, the NAP does not indicate how this is to be implemented. On education and training for IPC professionals, the NAP indicates it wants to achieve a good level of knowledge on infection prevention and antibiotic resistance among doctors, nurses, caregivers and paramedics through, amongst other measures, training. On monitoring and auditing for IPC practices, the NAP includes the development of a surveillance system of antibiotic use in relation to the disease, and the status of infection prevention in all healthcare networks that is uniform and reproducible, to which all healthcare providers provide data. Further, the NAP strongly advocates for innovation.
To promote the development of innovations in IPC, it proposes a new ZonMw antibiotic resistance programme and provides examples of innovative interventions.

IPC for animal health is barely included in the NAP. Specifically, policies and national legislation, initiatives to encourage livestock keepers to have a farm health plan, and national control and eradication programmes of specific animal diseases are not mentioned. The NAP does refer to supporting research on improving the health of livestock. The NAP also aims to improve general animal health in order to achieve extremely limited antibiotic use in animals.

### 5. Strengthen infection prevention and control measures

#### 5.1 Human healthcare IPC measures

- **5.1.1** Existence of IPC programmes at national level including national IPC guidelines
- **5.1.2** Education and training for IPC professionals
- **5.1.3** Monitoring and audits of IPC practices

#### 5.2 Animal health IPC

- **5.2.1** Policies and national legislation includes prevention measures in livestock, aquaculture [and pets]
- **5.2.2** Existence of initiatives to encourage/incentivise livestock keepers to have a farm health plan, as part of an integrated approach to on-farm animal health
- **5.2.3** National control and eradication programmes of specific animal diseases, other than those under EU legislation

### Prudent use of Antimicrobials in Human Health and Animals

Restriction of the use of certain antimicrobials and adoption of ‘AWaRe’ classification of antibiotics in the national essential medicines list are not specifically detailed in the NAP. One of the NAP’s objectives is to ensure that each healthcare facility establishes who is responsible for implementing and coordinating AMS programmes. It also plans for active monitoring of AMS, prescribing behaviour, and policies during outbreaks. The Health Care Inspectorate (IGZ) is responsible for the monitoring. The previously described surveillance system of antibiotic use also facilitates prudent use. At the international level, plans include the development of a roadmap by RIVM and WHO EURO that would support countries in the development of tailored interventions on prudent antimicrobial use (Guide to Tailoring AMR Programmes - TAP), or a plan to address gaps in the global agenda on the development and proper use of new resources.

In its annex, the NAP refers to multiple plans for the use of antibiotics in animals and farming, though details are lacking. The NAP has also set goals to further reduce the use of antibiotics in animals in order to limit the development of resistance where possible. This includes implementation of additional measures by the sectors and veterinarians, and further reducing the use of critical antibiotics. To this end, the NAP formulates the following activities: the continuation of more stringent inspections by the Netherlands Food and Consumer Product Safety Authority (NVWA); enforcement of restricted antibiotic use in animal farming; identification and control of illegal activities; and the improvement of general animal health in order to achieve extremely restricted antibiotic use. At EU level, the focus is on reducing or prohibiting the use of critical and last-resort antibiotics in animals.
6. Prudent use of antimicrobials

6.1 Optimising antimicrobial use in human health

6.1.1 Existence of specific measures to restrict the use of certain antimicrobial agents in humans

6.1.2 Existence of antimicrobial stewardship programmes at different levels

6.1.3 Adoption of ‘AWaRe’ classification of antibiotics in the National Essential Medicines List

6.2 Promote prudent use of antimicrobials in animals

6.2.1 Existence of treatment guidance developed taking into account the importance to preserve the efficacy of certain antimicrobials crucial to human medicine

6.2.2 Existence of specific measures restricting use of antimicrobials crucial to human medicine

6.2.3 Existence of measures to measures discourage inappropriate use of antimicrobials in animals

6.2.4 Existence of national legislation/policies to discourage inappropriate prophylactic and metaphylactic use of antimicrobials in animals (prior to new EU VMP & MF Regulations becoming applicable in 2022)

Investment/Research Programmes in the Area of AMR

The NAP has a strong focus on innovation. Its focus is on the development of new antibiotics, diagnostics and treatments, including alternatives to antibiotics, by strengthening research infrastructure and public-private partnerships (PPPs). The plans also include (financial) support to WHO to strengthen global collaboration and implementation of the GAP. In addition, the NAP proposes a fairly broad set of measures in its research strategy, with the aim to support and collaborate in international initiatives designed to develop new business models on antimicrobials. Plans also include identification of main bottlenecks in research and development, and marketing authorisation processes to facilitate development. Further, the NAP also promises to further support the development of scientific knowledge on antimicrobials and AMR through ZonMW and through continued participation in the European Joint Programming Initiative (JPI) on AMR. Last, the NAP also puts focus on alternative treatments and IPC.

7. Investment/research programmes in the area of AMR

7.1 Investment/research programmes in the area of AMR

7.1.1 Investment/research programmes to support the development of new medicines, diagnostic tools and vaccines (national)

7.1.2 Investment/research programmes in other areas

7.1.3 International collaborative work on research or other areas linked to AMR

Availability of New and Old Antimicrobials

As mentioned in the previous section, the NAP proposes to promote the development of new antibiotics, diagnostics and new treatments, and also aims to accelerate the antibiotic registration process by identifying and resolving bottlenecks in the regulatory process, and promoting the development of new business models for antibiotic development in international initiatives. Further, the NAP aimed to promote international research on new resources and prudent use through encouraging participation in Horizon2020 (EU wide research programme),
the Innovative Medicines Initiative (PPP programme), and supporting participation in the JPI by other (non-EU) member states. However, Horizon2020 is a previous iteration of the current Horizon Europe initiative, highlighting the outdatedness of the NAP. No mention is made of monitoring shortages of off-patent antimicrobials or of national stockpiles of crucial antibiotic agents.

8. Availability of new and old antimicrobial agents

8.1 Investment/research programmes in the area of AMR

| 8.1.1 | National incentives to develop and keep on market antibiotic agents |
| 8.1.2 | Support to manufacturers or suppliers of antimicrobials |
| 8.1.3 | Monitoring of shortages of off-patent antibiotics |
| 8.1.4 | Existence of national stockpiles of crucial antibiotic agents |

RECOMMENDATIONS

The reported increase of AMR incidence in the Netherlands and 30,000 deaths per year in the EU should be a matter of concern for everyone, and public authorities should address the issue as a fundamental threat to public health and welfare. As the Netherlands’ current NAP was developed in 2015, a review and update of the NAP is long overdue. To do so through a participative process with the involvement of relevant public, private and civil society stakeholders, and affected parties is a welcome step.

Recommendations to strengthen the next iteration of the NAP are found below:

- The WHO GAP on AMR should be used to structure the NAP. While the Netherlands is doing much in the fight against AMR, and performing well compared to other countries, the current NAP does not capture this fully. It is therefore recommended that the next iteration of the NAP should ensure all the Netherlands’ efforts on AMR, across all sectors and at the national, regional and global levels, are clearly described and outlined. This will facilitate collaboration between and across sectors and levels, while the NAP would at the same time function as a best-practice example for other countries.

- Outcome indicators covering different facets of antibiotic use and resistance, AMS and IPC should be developed and included in the next iteration of the NAP. New indicators and targets should be added, covering, for example, the number of antibiotic prescriptions per 1000 inhabitants per year in primary care (target: less than 250), or the proportion of children treated with third generation cephalosporins per year, out of the total number of children receiving antibiotics in primary care (target: less than 3%). A multi-year strategy should be included to reach set targets.

- Policies on the monitoring and combatting of the unregulated sale of antimicrobials, including online sales, and especially of substandard and falsified antibiotics, should be included in the NAP.

- Include periodic reviews of the progress made on targets set within the NAP and make these publicly available.

- While the 2015 NAP embraced the One Health approach, it did not integrate the necessary ICMs, both between public institutions and other stakeholders. Formal collaboration between actors is necessary to boost the effectiveness of public
interventions on AMR as well as other public health goals. It is recommended that formal collaborations are clearly outlined in the NAP, and that responsibilities for each ICM actor are clearly defined.

- Environmental monitoring is critical for effective implementation of a One Health approach; monitoring and surveillance of AMR should go beyond (waste) water to also include monitoring and surveillance of agricultural land and pharmaceutical production sites.

- In order to fully realise a One Health approach, engagement with all professional actors involved in the fight against AMR, including veterinaries, farmers, public health officials, pharmaceutical representatives, healthcare professionals and civil society, is recommended for the development of public awareness campaigns. Clear policies and targets for capacity-strengthening and (continued) professional education in the human health, animal health, and environmental sectors are also needed.

- A coordination mechanism should be developed that facilitates the collaboration between ZonMw, RIVM, and Dutch universities which addresses the challenges of AMR and opportunities for development of new antimicrobials in their syllabi and research programmes.

- Prudent use of antibiotics should be extended through the combined actions of a wide range of healthcare professionals: from primary healthcare doctors to prescribers, nurses and other medical professionals. Further, the NAP should include more details on its policies regarding the prudent use of antimicrobials in animals and farming.

- IPC measures should be fully integrated and funded not only as part of the fight against AMR but also because it is a general public health threat. An amended NAP should necessarily include IPC guidelines to be implemented in and disseminated through healthcare centres and residences.

- IPC measures in animal health were barely described in the 2015 NAP. While the Netherlands may have these IPC measures, it is important to also include and describe these in the NAP. The 2015 NAP described research activities that would be undertaken; this new version should include the necessary policy and legislative changes resulting from this.

- The availability of new and old antimicrobials is increasingly in jeopardy due to shortages and other market disruptions. The government needs to demand that pharmaceutical companies ensure the regular supply of all registered antimicrobials, and fine or bring to court those that fail to do so.

- In pursuit of the development of new and effective antibiotics, the Netherlands should support initiatives that seek to de-link the development of new medicines from their price, through push and pull mechanisms or advanced procurement agreements. The negotiation of the Review of the European Pharmaceutical Strategy is a good opportunity to frame the discussion away from intellectual property (IP)-driven market exclusivities.

- At the global level, the Netherlands must continue to support research activities on AMR by, for example, continuing its support to Horizon Europe and EU4Health. It should also continue to support the efforts of the Quadripartite and the Antimicrobial Resistance Multi-Partner Trust Fund, as well as the EU Joint Action on Antimicrobial Resistance and Healthcare-Associated Infections, the EU Joint Action on Surveillance, and the One Health European Joint Programme (2018–2023).
REFERENCES