



INTERAGENCY ASSESSMENT

EC/ECDC/EFSA Country visit to North Macedonia to advance One Health responses against antimicrobial resistance

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This report was commissioned by ECDC, coordinated by Aikaterini Mougkou (ECDC, country visit team lead) and produced by the consortium representatives Jean-Baptiste Ronat (Integrated Quality Laboratory Services) and Camelia Savulescu (Epiconcept). The European Commission's Directorate-General for Health and Food Safety (DG SANTE), European Food Safety Authority (EFSA) and a national expert from Czechia also contributed to its content.

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Contents

| | |
|---|----|
| Abbreviations | iv |
| Summary | 1 |
| 1. Introduction | 2 |
| 2. Objectives and scope..... | 3 |
| 3. Background | 4 |
| 4. Observations and conclusions..... | 5 |
| 5. Conclusions | 18 |
| 6. Considerations for future actions | 20 |
| References | 25 |
| Annex 1. Agenda of the country visit | 27 |
| Annex 2. List of ECDC antibiotic awareness materials to be translated by ECDC into Macedonian and Albanian for potential use in North Macedonia | 33 |

Abbreviations

| | |
|--------|---|
| AMR | Antimicrobial resistance |
| AMS | Antimicrobial stewardship |
| ASP | Antimicrobial stewardship programme |
| AST | Antimicrobial susceptibility testing |
| CAESAR | Central Asian and European Surveillance of Antimicrobial Resistance |
| ECDC | European Centre for Disease Prevention and Control |
| EFSA | European Food Safety Authority |
| EU/EEA | European Union/European Economic Area |
| EUCAST | European Committee on Antimicrobial Susceptibility Testing |
| FVMS | Institute of Food and Veterinary Medicine-Skopje |
| GLASS | Global Antimicrobial Resistance and Use Surveillance System |
| HAI | Healthcare-associated infection |
| HIF | Health Insurance Fund |
| ICU | Intensive care unit |
| IPC | Infection, prevention and control |
| NAP | National Action Plan |
| MIC | Minimum Inhibitory Concentration |
| VMP | Veterinary medicinal product |
| WHO | World Health Organization |

Summary

The European Centre for Disease Prevention and Control (ECDC), the European Commission's Directorate-General for Health and Food Safety and the European Food Safety Authority (EFSA) jointly carried out this country visit to North Macedonia from 29 January to 2 February 2024, which was coordinated by a consortium composed of Epiconcept and Integrated Quality Laboratory Services. The visit was part of activities to contribute to the advancement of the One Health approach against antimicrobial resistance (AMR) in the Western Balkans funded by the Directorate General for Neighbourhood and Enlargement Negotiations of the European Commission.

The report concludes that the current AMR situation in North Macedonia represents a serious patient safety issue that needs to be addressed as an urgent public health priority. Only a limited number of activities have been initiated to address AMR issues in the human health, animal health and food safety sectors. Implementation of the National Action Plan (NAP) on AMR 2019-2023 was delayed because of the COVID-19 pandemic and a multi-sectorial commission for control of AMR was only recently established with the task to update the NAP and start its implementation. The upcoming update of the NAP is an opportunity for the development of a comprehensive operational NAP, including all relevant actions, clearly delineating roles and responsibilities and supported by a dedicated budget and a defined timeline. Transparent and regular public reporting should ensure accountability and engagement across all relevant political levels.

In the human health sector, alarmingly high rates of multidrug resistance among various bacterial species indicate that transmission within healthcare settings remains the main driver. The level of inappropriate use of broad-spectrum antibiotics, combined with inadequate infection prevention and control (IPC) practices, intensifies the problem. Furthermore, adherence to evidence-based treatment guidelines among doctors is suboptimal across both community and hospital settings. Specifically, the management of infections in hospitalised patients predominantly relies on empirical antimicrobial treatment rather than on diagnostic test results, such as blood cultures and antimicrobial susceptibility tests. The lack of surveillance data to describe the local AMR epidemiology at each healthcare facility hinders doctors' ability to make informed prescription decisions, ultimately impacting patient outcomes. Limited expertise and lack of resources and allocated time for antimicrobial stewardship (AMS) activities exacerbate the overuse and misuse of antimicrobials, as there is no supervision of prescriptions and support in de-escalation of unnecessary broad-spectrum antibiotic treatments. Urgently developing the NAP, strengthening IPC and antibiotic stewardship programmes (ASPs) in hospitals, especially in the intensive care units (ICUs), by ensuring appropriate human and financial resources for sustainable implementation of interventions and establishing surveillance on AMR, HAIs, IPC practices and antibiotic consumption should be the priorities for the Multi-sectorial Commission for Control of AMR.

In the animal health and food safety sector, the Institute of Food and Veterinary Medicine (FVMS) in Skopje is the official reference laboratory for AMR established connections with European Union (EU) laboratories and quality assurance measures. North Macedonia actively participates in EU harmonised monitoring efforts but faces challenges in obtaining the required number of samples and isolates, hampering the assessment of the AMR picture in the sector. While the sampling coverage and the number of isolates tested may not yet be fully compliant with EU requirements, there is a good disposition to investigate and scale up the efforts. The country has conducted a few point prevalence surveys on AMR in veterinary pathogens but increasing the number of such studies would improve coverage and understanding of this issue. Although legal requirements for reporting data on imports and sales of veterinary medicinal products (VMPs) are in place, deficiencies in validation methods and tools hinder data completeness and accuracy. Limited capacity for data collection on antimicrobial use, lack of awareness among many veterinarians and farmers, logistical difficulties in laboratory testing for performing sensitivity tests for clinical isolates, and pressure to prioritise broad-spectrum antibiotics pose challenges for effective antimicrobial stewardship efforts. Although some prudent use initiatives exist, further actions are needed to address the overuse and misuse of antimicrobials in the animal health and food safety sector. The Food and Veterinary Agency (FVA) has demonstrated proactive efforts in publishing guidelines, including on the responsible use of antimicrobials in food-producing animals, and initiated training activities, but gaps in awareness and communication among practising veterinarians persist. Ongoing education and awareness initiatives are essential to address knowledge gaps and foster behaviour change among stakeholders. Despite recognising the need for legislation to prevent environmental contamination, safe disposal routes for expired and unused medicines are lacking. There is no regular monitoring of the presence of antimicrobial residues, antimicrobial-resistant bacteria and AMR genes in the environment, which hinders effective situation assessment and planning of further interventions.

Continued efforts and renewed and long-term sustained commitment from ministries at the highest level need to be consolidated to effectively address AMR through surveillance, prudent use of antimicrobials in all sectors, urgent implementation of IPC measures and increasing awareness of public and health professionals. The commitment of stakeholders in all sectors, ministries and agencies is essential to develop and implement the new NAP using the One Health approach. In this report, several initial recommendations are provided which could serve as a starting point to develop a more specific One Health roadmap to combat AMR in North Macedonia.

1. Introduction

Antimicrobial resistance represents a serious threat to people's health and to economies around the world. Recent estimates of the burden of AMR in the World Health Organization (WHO) European region indicated that, in 2019 alone, nearly 700 000 deaths were associated with or attributed to bacterial AMR [1]. A study estimated that between 2016 and 2020 in the European Union and European Economic Area (EU/EEA), 70% of antibiotic-resistant bacterial infections were healthcare-associated infections (HAIs), and the number of deaths ranged from 30 730 in 2016 to 38 710 in 2019 [2]. With the current increasing trends of AMR, it also has significant costs, especially for healthcare systems, which could cost the world economy up to 100 trillion USD by 2050 [3].

In line with the Global Action Plan on AMR [4], adopted in May 2015 by the World Health Assembly and subsequently by the World Organisation for Animal Health and the Food and Agriculture Organization, the European Commission published its own [EU One Health Action Plan against AMR](#) in 2017. The key objectives of this plan are built on three main pillars:

- making the EU a best-practice region;
- boosting research, development and innovation;
- shaping the global agenda.

As part of this agenda, and more specifically the third pillar, the EC commits to supporting candidate countries for accession to the EU in aligning and implementing the EU legislation on AMR.

One of the five strategic objectives of the ECDC Strategy 2021-2027 [5] is dedicated to increasing health security in the EU through international collaboration and alignment regarding infectious disease policies and practice by strengthened cooperation and coordination between ECDC and partners in non-EU countries, especially EU enlargement countries. On 10 December 2019, the EU Contribution Agreement No 2019/409-781 was signed between ECDC and the European Commission and amended on 23 December 2020 to implement the ECDC Action 'Preparatory measures for the participation of the Western Balkans and Türkiye in the ECDC with special focus on One-Health against AMR and enhanced severe acute respiratory infections surveillance, 2020 – 2024' (ECDC-IPA6 project) with external financial assistance under the Instrument of Pre-accession Assistance (IPA).

The Joint ECDC and EFSA regional workshop on the One Health approach against AMR for EU pre-accession countries, held in 2019 in Belgrade, Serbia, recognised an urgent need to boost the advancement of AMR responses and to attain a certain level of implementation of related EU legislation in the region [6]. National governments need to put in place regulatory requirements, necessary laboratory infrastructure and techniques, efficient comprehensive and interoperable electronic surveillance systems, training, additional human workforce in the human and animal health fields, as well as awareness raising and commitment to ensure sustainability of efforts.

Work Stream 2 of the ECDC-IPA6 project focuses on the advancement of a One Health approach against AMR in the Western Balkans. It includes One Health country visits to discuss AMR issues, identify gaps and support the development of roadmaps on AMR in different sectors: human health, animal health, food safety and the environment. In addition, to align with previous One Health country visits on AMR organised in the EU/EEA countries, the visits to countries under pre-accession assistance include experts from ECDC, the Directorate-General for Health and Food Safety and EFSA. The experts cover areas relevant for AMR surveillance, IPC and antimicrobial use under a One Health perspective.

2. Objectives and scope

The overall objective of this joint country visit to North Macedonia was to discuss and review the advancement of a One Health approach against AMR through:

- the identification of strengths and weaknesses in the current national AMR strategies, action plans and intersectoral coordination mechanisms;
- reviewing the capacity of the current laboratory network to detect AMR and resistance trends;
- documenting the situation and efforts being made on AMR surveillance, antimicrobial consumption (AMC) and HAIs;
- reviewing actions related to the prudent use of antibiotics in human health, animal health, food safety as well as in the environmental sector;
- reviewing activities and approaches to raise awareness regarding AMR.

A detailed agenda of this One Health country visit is provided in the Annex.

The visit focused primarily on the AMR governance and intersectoral mechanisms to implement the One Health approach against AMR in North Macedonia.

For the human health sector, the visit focused on:

- the laboratory capacity to process, collect and share AMR data at the national and local level;
- monitoring activities on AMR and AMC;
- antimicrobial stewardship (AMS), treatment guidelines and prudent use of antimicrobials;
- IPC;
- communication, behavioural change interventions and awareness activities.

The evaluation and discussions on the human aspect of AMR were guided by the assessment tool developed by ECDC [7].

For the animal health and food safety sectors, the visit focused on:

- the policies to tackle AMR through the reduced and more prudent use of antimicrobials in animals;
- monitoring of AMR in animals and food;
- laboratory capacity to generate AMR data;
- surveillance of antimicrobial sales and use in the veterinary sector;
- communication and awareness activities.

To a limited extent, the visit also covered environmental aspects of AMR such as the disposal of expired and unused drugs in the food production sector.

3. Background

North Macedonia is a member of the WHO Regional Office for Europe and of the Central Asian and European Surveillance of Antimicrobial Resistance (CAESAR) network established in 2013. In the latest CAESAR report with AMR surveillance data in Europe for 2021, North Macedonia had high geographical hospital representativeness but low representativeness of isolates and a low blood culture rate (4 per 1 000 patient-days reported in 2018). High levels of AMR were reported for most of the pathogens from bloodstream infections [8]. North Macedonia was among the countries that reported more than 50% resistance of *Escherichia coli* to fluoroquinolones and to third-generation cephalosporins, of *Klebsiella pneumoniae* to third-generation cephalosporins and of *Enterococcus faecium* to vancomycin (compared to 34% or less for the EU/EEA) [8].

In 2021, North Macedonia was the country in Eastern Europe with the lowest proportion (26%) of antibiotics from the 2019 WHO essential medicine list that were included in the national essential medicine list. According to the same report, only six out of the 19 Access antibiotics were included in the national essential medicine list [9]. WHO estimates that the total consumption of antibiotics in North Macedonia significantly exceeds the European weighted mean of 21.9 DDDs/1 000 inhabitants/day approaching 35 DDDs/1 000 inhabitants/day [10].

A study on the sales of antiviral and antibacterial agents from community pharmacies during the COVID-19 pandemic over one week in Skopje and four other regions outside of Skopje (56 private pharmacies) indicated a high (97.1%) supply related to the presentation of prescriptions [11]. Almost all were oral formulations (99.2%) and 96% were categorised under the ATC group J01. The most common indication of treatment was upper respiratory tract infection (URTI, 54.8%), followed by COVID-19 (12.7%), while influenza was the indication for 1.8% of antibiotic treatments. The most common antibiotic for URTI was azithromycin, followed by amoxicillin with beta-lactamase inhibitor and cefixime. Azithromycin was also the most common antibiotic when the indication was influenza. The most supplied antibiotic related to hospital care was ciprofloxacin.

A study [12] on the knowledge, attitudes and behaviours on AMR among the general public across 14 Member States in the WHO European region, including North Macedonia, was conducted in 2022. Of 556 participants in North Macedonia, 53% reported taking antibiotics in the past year, higher than the EU average of 23% [13]. Most participants received antibiotics through prescription or directly administered by a practitioner (86%), with 7% buying them without prescription. Interestingly, 67% had a blood or urine test or throat swab before starting antibiotics, higher than the EU average (53%). Doctors were the main source of information against unnecessary antibiotic use (81%), followed by internet/social networks (30%) and pharmacists (23%). Many participants expressed a need for more information on antibiotic use (47%) and related medical conditions (39%).

In the veterinary and food production sectors, the responsibility to address AMR as well as antimicrobial sales and use issues has been assigned to the Food and Veterinary Agency (FVA). The FVA carries out official controls at distributors (importers) of veterinary medicinal products (VMPs), veterinary practices, veterinary pharmacies, and farmers. The FVA is also an inspection body, which conducts inspections in the field of safety, hygiene, traceability and labelling of food and feed. Regarding AMR, in collaboration with the FVA, the Food Institute of the Faculty of Veterinary Medicine-Skopje is responsible for performing AMR surveillance following the EU harmonised AMR monitoring in zoonotic and commensal bacteria in certain food-producing animals and food.

4. Observations and conclusions

4.1 Antimicrobial resistance strategies, action plans and coordination, based on a One Health approach

4.1.1 Multi-sectoral collaboration and coordination

The Multi-sectoral Commission for Control of Antimicrobial Resistance was established in 2009, re-appointed in November 2018, and had its last meeting in November 2019. During the COVID-19 pandemic, it demonstrated only limited activity. During the country visit, reports detailing the progress of previous activities were unavailable. However, former members of the Commission indicated that some activities had been initiated. The Commission had reconvened on 13 December 2023 and met three times before the country visit. No minutes of these meetings were presented to the visiting team.

The current Commission comprises 22 members from relevant institutions: Institute of Microbiology and Parasitology (IMP, President of the MCCAMR), Institute of Public Health (IPH, National Coordinator of the AMR Programme), representatives from the Ministry of Health, the Ministry of Agriculture, and the Ministry of Environment, representatives from the Sanitary Health Inspectorate and the Medical Board and Infectious Diseases Association, the National tuberculosis coordinator, representatives from the Faculty of Veterinary Medicine-Skopje (FVMS), the Health Insurance Fund (HIF), representatives from Food and Veterinary Agency (FVA), and WHO Country Office representatives.

Their tasks include the development of the new National Action Plan (NAP) with policy recommendations addressing AMR, as well as overseeing the implementation of One Health activities through working groups. They aim to foster collaboration between ministries, agencies and organisations to mobilise resources effectively as well as support the development of electronic surveillance.

The detailed terms of reference of the Commission with the scope, responsibilities, expected outcomes, and resources still need to be defined and a timeframe were not provided. Previous iterations of the Commission functioned voluntarily without an allocated budget, and the current one does not have specific financial resources or protected dedicated time allocated to its members.

4.1.2 National strategies and action plans on antimicrobial resistance

The National Strategy for control of AMR and related NAP for 2019-2023 followed the NAP 2012-2016. The general objective of the NAP 2019-2023 was to improve the health of the population in North Macedonia through the control of AMR, thus preserving the effectiveness of antimicrobials. There were seven strategic objectives:

- Strengthen the monitoring of microorganisms resistant to antimicrobials and provide evidence-based data on AMR in human and veterinary medicine;
- Continuously monitor the consumption of antimicrobials in human and veterinary medicine;
- Prevent and control HAIs;
- Promote the rational use of antimicrobials in human and veterinary medicine;
- Raise awareness and understanding of AMR in those who prescribe, issue and receive, or use antibiotics;
- Promote cooperation with institutions with expertise in AMR, such as the ECDC, WHO, the World Organisation for Animal Health, and others;
- Monitor and participate in developing and discovering new antimicrobials, introducing new diagnostic procedures and other interventions.

The NAP was written from a One Health perspective; however, the implementation of the activities was put on hold due to the COVID-19 pandemic.

The NAP 2019-2023 budget was to be derived from participating governmental institutions (e.g., annual public health programmes, participating ministries' budgets) and technical assistance from WHO and EC. However, no accounting report on the use of the budget was available during the country visit.

All professionals who met during the country visit unanimously agreed that the NAP needs updating, and this should be the main task of the newly appointed Multi-sectoral Commission for Control of Antimicrobial Resistance.

4.1.3 Conclusions

The Multi-sectoral Commission for Control of Antimicrobial Resistance has been recently established, but its Terms of Reference with defined roles, responsibilities, and dedicated time and budget need to be developed. A new NAP should urgently be developed including structure, process and outcome indicators, as well as targets to be achieved. Activities and relevant entities for both the human and animal health sectors should be involved to ensure the transversal, One Health nature of the NAP. To fulfil these objectives, specific funding must be secured for each activity in the NAP. The Commission would benefit from expertise from different fields currently not represented in its structure, such as IPC experts, and should become aware of all initiatives related to AMR in the country and reassemble and integrate these initiatives into the new NAP.

The NAP 2019-2023 concluded that most of the listed activities were not implemented. Hence, there is an urgency for the newly appointed Commission, which is politically supported by the relevant ministries, to formulate and implement a new enhanced NAP using the One Health approach. The new NAP would benefit from high-level political endorsement that would ensure financial and human resources for its implementation.

4.2 Human health aspects of antimicrobial resistance

4.2.1 Organised multidisciplinary collaboration at the local level

At present, there is limited expertise on antimicrobial stewardship and IPC (except in one private hospital visited) and close collaboration among various disciplines (e.g. epidemiologists, clinicians, nurses), both locally and nationally. The ECDC team did not detect any active multidisciplinary teams (pharmacist, microbiologist, infectious diseases physician, IPC specialist) dedicated to specific surveillance and intervention programmes in most of the visited healthcare facilities. There was a lack of engagement in collaborative efforts toward common objectives and initiatives, such as the systematic collection, analysis and interpretation of local data, as well as its translation into actionable insights for public health interventions. No established link between surveillance activities in primary and hospital care was identified during the visit.

Senior managers are mainly involved in reporting the number of positive blood cultures (mandated by national legislation) while their engagement in actively supporting activities related to IPC, AMR monitoring, or AMS at their healthcare facility is limited, except in a private hospital and a geriatric/long-term healthcare facility visited by the ECDC team.

There is no established collaboration between primary and secondary care regarding the prudent use of antibiotics. The continuity of primary care for the elderly is frequently disrupted when there is a change of general practitioner (GP) upon admission to a long-term care facility. In some cases, GPs may find it necessary to adjust diagnoses to align with specialists' antibiotic prescriptions to ensure reimbursement.

At the local level, the ECDC team observed a few examples of good collaboration between microbiologists and clinicians in reporting test results of antimicrobial-resistant infections and, in one visited facility, between the clinical pharmacists and clinicians for antimicrobial use. This was mainly based on the personal relationships between colleagues working in the same visited clinic/hospital. Establishing a standardised implementation of this approach is crucial for the proper management of patients.

4.2.2 Clinical diagnostic and reference laboratory services

There is no officially appointed National Reference Laboratory for AMR in human health with the capacity for second-line or confirmatory species identification and antimicrobial susceptibility testing (AST) of bacterial or fungal organisms. The IPH's microbiology laboratory routinely performs microbiology analyses on clinical samples from patients using conventional identification methods as well as the automated VITEK® 2 compact system. It performs AST using the Kirby-Bauer disc diffusion method according to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) standard or the VITEK® 2 compact system. The IPH laboratory cannot perform PCR for AMR gene detection and, while access to whole genome sequencing equipment (one Illumina sequencer and one GridION) is available, it is not used for bacterial whole genome sequencing due to a lack of consumables and trained staff. The laboratory at IPH cooperates with the National Veterinary and Food Institute¹ from the FVMS in Skopje, to identify organisms using MALDI-TOF, which is available at the National Veterinary and Food Institute. Regarding AMR-related external quality assessment schemes, the laboratory at IPH participates in the CAESAR international external quality assessment exercises. It also participates in similar exercises with UK-NEQAS microbiology.

¹ As of 1 March 2024, the Veterinary Institute, the Food Institute and the Institute for reproduction and biomedicine became the National Veterinary and Food Institute

There are about 27 laboratories in North Macedonia (the number is subject to frequent change due to small laboratories) that can perform clinical microbiology testing to identify bacterial pathogens and perform AST. Sixteen of these laboratories are public institutions and 11 are private. Three of these 11 private laboratories are part of private hospitals.

The microbiology laboratory at the IPH coordinates the implementation of a laboratory information management system to facilitate the analysis of AMR data and trends. This laboratory information management system will be deployed across the network of regional public health laboratories allowing real-time sharing and central analysis of laboratory results.

The Institute of Microbiology and Parasitology (IMP), located in Ss Cyril and Methodius Teaching Hospital, has its own microbiology laboratory and provides clinical microbiology services to neighbouring healthcare facilities, too. In contrast, regional public health institute laboratories provide clinical microbiology services to the regional hospitals. None of these laboratories transfer isolates of multidrug-resistant bacteria (e.g. carbapenem- and/or colistin-resistant Enterobacterales, carbapenem-resistant *Acinetobacter baumannii*, carbapenem-resistant *Pseudomonas aeruginosa*, vancomycin-resistant *Enterococcus* and methicillin-resistant *Staphylococcus aureus* and other EARS-Net priority pathogens) to the microbiology department at the IPH for confirmatory testing. We noted that laboratory capacity is overall underutilised, with extremely few blood cultures being performed. For instance, the visited Public Health Laboratory in Kumanovo receives only about 10 blood culture bottles per month; the IMP receives an average of 200 blood culture bottles per month; and the microbiology department at the IPH an average of 60 blood culture bottles per month.

Laboratory results that are critical for patient care are promptly communicated to clinicians, so they are useful for patient management decisions. Pathogen identification from blood cultures is communicated to clinicians in a timely fashion, i.e. on initial positivity and when preliminary species identification is available. Gram staining is systematically performed on positive blood cultures or cerebrospinal fluid samples. Clinicians confirmed that they usually receive laboratory results promptly. A hospital health management system to link laboratory data to patient records was in place in all visited hospitals. Laboratory results are sent electronically via this system but can also be collected by healthcare staff (paper-based), while preliminary positive results are provided directly by phone. Out-of-hour microbiology services were not available. Laboratories close at 14:00 on working days (Monday–Saturday) and neither microbiology samples are accepted, nor microbiology expert advice is provided after this time. On Sundays, routine microbiology tests were not performed in any of the visited public health laboratories. Finally, point-of-care tests or rapid diagnostic tests, such as urine strips, C-reactive protein and Group A *Streptococcus* tests, were not accessible in hospitals or primary healthcare facilities.

According to microbiologists from the IPH, all public health laboratories are using EUCAST standards for AST. Testing for colistin susceptibility is performed according to EUCAST recommendations using a broth microdilution method. According to microbiologists at the IPH, no other guidelines for AST are used in all clinical microbiology laboratories in the countries.

4.2.3 Monitoring of antimicrobial resistance

At the national level, communicable disease surveillance is based on the 'Law on Protection Against Communicable Diseases' from 2008, including subsequent amendments, with the last amendment published in the Official Gazette of North Macedonia in 2020 to include COVID-19 in the list of notifiable diseases. The current law includes 64 diseases and 56 pathogens under surveillance with mandatory notification. This law stipulates that intrahospital infections (defining them as infections time-bound with treatment and stay in healthcare facilities) and any infectious diseases outbreak as well as 'every case of isolated bacteria with unusual resistance to antibiotics' are subject to mandatory reporting. This approach to surveillance results in a very heterogeneous system. The current law on protection against communicable diseases is under revision, so it is aligned with EU legislation especially concerning the list of diseases under mandatory notification, as well as strengthening the national early warning and notification system.

Enforcement of the 'Law on protection against communicable diseases' is based on various rulebooks that provide further details for disease notification, case definitions and the prevention and control of HAIs:

- Rulebook on reporting, format and content of the reporting forms for communicable diseases and microbiological agents: the last update of this Rulebook was in 2009. This Rulebook stipulates that each healthcare facility or laboratory that detects a positive culture with a notifiable pathogen and has performed AST must report the findings. The specific AMR profile is reported on a separate form. For the notifiable diseases, a case-based report is submitted electronically by clinicians based on clinical criteria and microbiological results, if available. Laboratories should report all positive results of the listed pathogens, regardless the clinical findings. All national laboratory experts mentioned that no clinical criteria are provided, and they only report positive cultures.

- Rulebook on the criteria for case definitions of communicable diseases: it was adopted in 2018, based on the EU case definitions of 2012 [14]. This includes the case definitions of HAIs based on the European Commission Implementing Decision, but a limited understanding of these case definitions was observed among the experts met by the visiting team.
- Rulebook on the detailed criteria for the prevention and control of HAIs.

All laboratories report priority bacteria and AMR based on the CAESAR and the Global Antimicrobial Resistance and Use Surveillance System (GLASS) protocols. The microbiology department at the IPH collects the data on a national level and reports to CAESAR and GLASS. No analyses of national data are performed at the IPH and no collaboration with epidemiologists was noted at the IPH. Feedback received from CAESAR and published annually by WHO/ECDC/RIVM on the reported data is made available to reporting laboratories.

There is limited use of IT tools for reporting surveillance data, analysis and feedback. The laboratory and surveillance data are not integrated. The available data are not analysed and translated into public health messages and opportunities. More importantly, data are not used to provide feedback to clinicians and to inform optimal management of patients according to local/hospital/ward epidemiology.

Epidemiologists from the ten public health centres send the case-based and isolate-based paper forms to the IPH. Data are entered manually into a database and aggregated at the central level. A national compilation is done quarterly and annually by aggregating the data received from the ten centres. No trend analysis or additional analyses are performed based on the HAI or AMR reports.

The pathogens *K. pneumoniae*, *Acinetobacter baumannii* and *Enterococcus* spp. are not included in the list of pathogens that need to be reported. However, they could be reported under the criteria of 'any unusual AMR pattern'. The visiting team could neither identify any specific AMR surveillance or projects in place for other pathogens included in the list such as *Neisseria gonorrhoeae*, *Campylobacter* spp., *Salmonella* spp. and *Shigella* spp., nor for emerging pathogens with AMR (e.g. *Candida auris*) or AMR genes (e.g. carbapenem resistance genes). For tuberculosis, surveillance and AST is performed at the laboratory of the Institute for Pulmonary Diseases and Tuberculosis at the University Clinical Centre 'Mother Theresa' which was not visited. Data on multidrug-resistant and extensively drug-resistant tuberculosis are not integrated with AMR data from general communicable disease surveillance.

AMR surveillance activities in the community (e.g. surveillance of AMR in *S. pneumoniae* invasive isolates), if available, were not observed by the visiting team.

As mentioned in the CAESAR reports, the frequency for taking blood cultures is very low with a mean rate of 4 blood culture sets per 1 000 patients-days (range 0-40) in 2018, which undermines the representativeness of surveillance data, e.g. for surveillance of AMR in bacteria from bloodstream infections. This also suggests that the quality of clinical care for patients with severe infections may be suboptimal because most clinicians seem to resort to empirical treatment even for patients with life-threatening infections. Microbiology laboratories appear willing and have the expertise to perform AST on all samples; hence, the low number of tested samples may be related to the lack of test orders from clinicians. Barriers to requesting blood cultures were unclear, but those cited included the lack of clinical evidence-based protocols available to clinicians, limited availability of blood culture bottles, and financial pressure to contain costs in the clinical wards.

The healthcare professionals met by the visiting team are aware that AMR increased during the COVID-19 pandemic, especially in the surgical and neonatology units. They believe that the reason was increased AMC during the COVID-19 pandemic. AMR and AMC data are neither integrated and analysed, nor fed back to clinicians for AMS and IPC activities or used for designing public health interventions.

4.2.4 Monitoring of antimicrobial consumption

Three institutions share responsibilities in monitoring AMC in North Macedonia:

- The Macedonian Agency for Medicines and Medical Devices ensures that all medicinal products for human and animal use meet the quality, efficiency and safety requirements and monitors the wholesale for all products. This agency operates under the 'Law on medicines and medical devices'. The institution also comprises a team of six inspectors in charge of inspections of pharmacies and healthcare facilities.
- The Ministry of Health - Directorate on e-Health operates under the 'Law on Healthcare' and runs the national eRegister of medicines. The Ministry of Health is also in charge of developing therapeutic guidelines which should consider prudent use of all medicinal products, including antibiotics.

- The Health Insurance Fund (HIF) operates under the 'Law on Health Insurance' and monitors the use of medicinal products including antibiotics. The list of the medicines covered by the HIF is approved each year. The HIF has implemented the WHO methodology on AMC monitoring and surveillance [15] and, since 2011, has reported AMC data annually to WHO. The reports are available on the HIF website although the presented data are only based on the reports from the providers who have an agreement with HIF. These data are not integrated with other systems from the Macedonian Agency for Medicines and Medical Devices and the Ministry of Health (wholesales and products authorisation). The data are analysed according to the WHO AWaRe classification, a tool developed by the WHO to guide antibiotic use by categorising antibiotics into three groups (Access, Watch, Reserve) [16] or by broad-spectrum vs. narrow-spectrum antibiotic categories and presented in the AMC reports from WHO.

The three data collection systems on diagnosis-related groups (medical services) at the Ministry of Health/eRegister, prescriptions to insured patients (HIF) and wholesales of antimicrobials from both public and private institutions (the Macedonian Agency for Medicines and Medical Devices) are not linked to integrate the data collected.

Data on AMC are also collected at the healthcare level (hospitals and clinics visited) and pharmacists are aware of the type and quantity of antimicrobials used but this is done for procurement purposes and not for AMS activities such as feedback to prescribers. Notably, the WHO AWaRe (Access, Watch, Reserved) classification was less known at some hospital pharmacies visited.

AMC indicators such as the AWaRe classification and categorisation in broad- vs. narrow-spectrum antibiotics were not used to analyse, benchmark or feedback for improvement and other antimicrobial stewardship activities.

By law, antibiotics can only be obtained from pharmacies if the patient has a medical prescription. However, there is a difference in calculated AMC when using reimbursement data from HIF and wholesale data from the Macedonian Agency for Medicines and Medical Devices indicating possible over-the-counter sales of antibiotics in the country.

4.2.5 Antimicrobial stewardship and treatment guidelines

Antimicrobial prescribing guidelines for managing patients with infections were available on the Ministry of Health website. However, there was agreement among the professionals met by the visiting team that these guidelines need to be updated, made more widely known to clinicians and used in all healthcare facilities.

By law, each hospital is required to establish a committee dedicated to monitoring the use of antibiotics. Although some public hospitals have attempted to implement such initiatives since 2015, these efforts have largely failed. In the public hospitals that were visited, there was no evidence of active committees. In the visited private hospital, there was an AMS committee led by an infectious diseases specialist. The AMS committee monitors the antibiotics administered to hospitalised patients and intervenes if the treatment does not follow hospital protocols or international guidelines. The AMS committee includes a microbiologist, the IPC nurse, a clinical pharmacist, the chief nurse, an education nurse and other professionals, and a total of 18 members. Hospital protocols for different clinical conditions were shown to the visiting team. Blood cultures are taken according to the protocols and AST data on selected pathogens are sent to the IPH to be included in the CAESAR reports. In 2022, 97% of *Acinetobacter* spp. isolates were multidrug-resistant.

In public hospitals, medical doctors rarely order blood cultures, and this seems to be due to a lack of protocols for appropriate management of patients with suspected or confirmed infection. However, when microbiological samples (including blood cultures) are sent, the laboratory staff inform clinicians directly by telephone on the gram-stain results when positive, and later on the isolated pathogen. Microbiology samples, including blood cultures, can be sent to a clinical microbiology laboratory during weekends, but the results are only available the next weekday due to the lack of night/weekend shifts in clinical microbiology laboratories (see above).

Antimicrobials are acquired by each hospital through public procurement. If an antimicrobial is not included in the HIF list, the Ministry of Health and HIF must approve the procurement from the public funds allocated to the hospital.

In the community, significant overuse and misuse of antimicrobials were mentioned by the professionals met by the visiting team. Antimicrobials are often prescribed as multiple packages or bottles, enabling individuals to accumulate stocks of these medications at home and self-medicate with antimicrobials whenever they have a febrile illness.

4.2.6 Infection prevention and control

In adherence with the national Regulation on IPC, secondary and tertiary healthcare facilities should establish a multidisciplinary IPC committee. Notably, during the visit, the IPC committees within the visited facilities, except the private hospital, lacked dedicated personnel with the necessary IPC expertise. Nevertheless, within most of the visited hospitals, the IPC committees comprised enthusiastic healthcare professionals. According to the national Regulation on IPC, each IPC committee must include at least one medical doctor specialised in infectious diseases, epidemiology or microbiology and one nurse. In some of the visited public hospitals, the engagement of senior management in the work of the IPC committee appeared limited.

There was a common agreement among the national experts that HAIs are not reported or under-reported, while it was also evident that there is a lack of understanding on the precise definition of what constitutes a HAI. No systematic surveillance of HAIs, such as bloodstream infections, pneumonias, urinary tract infections and device-associated infections, was performed in any of the visited healthcare facilities.

The only HAI surveillance which is performed is a passive case-based reporting of isolates from blood cultures from secondary and tertiary care facilities to IPH. The national database made available to the visiting team included 316 and 622 cases in 2022 and 2023, respectively. Quarterly and annual reports were presented by the IPH, compiling data on isolates from bloodstream infections of hospitalised patients received from the 10 public health centres. No trend analyses or calculation of indicators are performed. It is not clear whether these reports are sent back to the hospitals who have provided the data.

As indicated by law, samples from environmental surfaces and from healthcare workers at different departments must be obtained regularly. Sampling is usually conducted by staff from the public health centres. In recent years, this has resulted in more than 7 000 samples in total and, in 2022, 116 samples were positive. It was unclear, however, how and whether these results were used for feedback to the facilities or healthcare workers.

There was no IPC programme, including guidelines, bundles, surveillance indicators, feedback and training in the visited healthcare facilities, except in the private hospital where the IPC programme had been implemented to comply with international accreditation requirements. Training of clinical staff on basic IPC and hand hygiene practices was mentioned at a visited secondary hospital and a geriatric clinic.

Hospital pharmacies keep registries of alcohol-based hand rub consumption, but this information was not used for IPC monitoring. Alcohol-based hand rub was not available at the point of care in most hospital areas, including the visited ICUs. Most of the hand washing sinks did not have disposable paper dispensers closely available.

There was a lack of systematic monitoring of compliance with standard precautions and hand hygiene practices in all visited facilities. The visiting team observed that many healthcare workers were not performing hand hygiene before contact with patients. In some of the visited facilities, many healthcare workers wore watches, jewellery and/or had long artificial nails, even in ICUs, which hinders the effectiveness of hand hygiene practices. The ICU bedheads with ventilated patients were not always elevated, and full urinary catheter bags were lying on the floor.

All visited public hospitals were understaffed, mainly regarding the patient-to-nurse staffing ratio. For example, in the ICUs, there was only one nurse for every four to five patients.

The Institute of Epidemiology and Biostatistics at the Faculty of Medicine of University Ss Cyril and Methodius, Skopje was funded under the National programme for Public Health 2023 to participate in HAI-Net surveillance of HAI in ICU and train healthcare workers on HAI monitoring and antibiotic use. No reports were made available to the visiting team, and it is not clear how these resources, if made available to the Institute, were used.

A national plan for patient safety is under development. The draft was not made available to the visiting team, but according to this plan, an electronic register of HAIs will be implemented.

The number of single rooms in most of the wards, including the ICUs, was not sufficient. In all visited ICUs, bed occupancy was mentioned as being high. However, during our visit to ICUs, the rooms were not fully occupied. It was mentioned that beds/areas of patients carrying multidrug-resistant bacteria are usually clearly marked, but we did not see any evidence of such a policy being implemented except in the visited geriatric clinic.

4.2.7 Educational programmes on antimicrobial resistance and infection, prevention and control

Antimicrobial resistance is not explicitly addressed as a specific subject during undergraduate medical school, but the principles are covered within relative topics (e.g. microbiology, pharmacology).

On one occasion, some undergraduate medical students were involved in activities on AMR prevention through the European Medical Students' Association programme, under the supervision of a microbiology professor from the University of Ss Cyril and Methodius (Skopje) who was previously the Multi-sectorial Commission for Control of AMR chairperson.

An online education course on AMR, mainly for primary healthcare providers, was held in 2023 offering continuous medical education (CME) credits. No such course was organised for nurses.

There is a mandatory CME programme for all physicians, who need to obtain 20 CME credits per year to keep their medical licence. However, the existing CME courses do not include topics such as IPC, AMR and AMS and therefore there is no opportunity for physicians to be educated on AMR-related topics.

In general, participation of doctors and nurses in continuous professional education activities and attendance at conferences appear to be predominantly sponsored by the pharmaceutical industry. Accumulation of credits through these activities does not appear to provide significant career benefits. Postgraduate courses and compulsory educational programmes focusing specifically on AMR, AMS and IPC tailored for medical doctors including residents, GPs and paediatricians, are currently lacking.

4.2.8 Public information and behavioural change interventions on antimicrobial resistance

All healthcare professionals met during the country visit mentioned the lack of knowledge of antibiotic use and AMR among the public. In all healthcare facilities and pharmacies that were visited where the public has access, there were no educational materials such as posters or leaflets for increasing awareness of AMR and inappropriate use of antibiotics.

The COVID-19 pandemic was often perceived as the main driver of increased AMC and AMR in recent years. However, no studies on behaviours, perceptions, cultural beliefs and attitudes for planning and implementing behaviour change interventions were presented to the visiting team. The only publication identified by the visiting team was related to the parents' attitudes toward antibiotic prescriptions in a study conducted in 2014 [17]. A nationwide and multifaceted intervention, including a mass media (television) campaign on appropriate antibiotic use, seminars in kindergartens and healthcare facilities, and reinforcing the restriction on over-the-counter antibiotic sales in pharmacies was introduced in 2014. The study concluded that the initial poor parental knowledge that antibiotics were not needed for viral infections did not significantly improve after the mass media campaign, and the legal penalties to discourage over-the-counter dispensing of antibiotics did not immediately reduce self-medication practices. In addition, the authors concluded that media campaigns need to be implemented for a longer period, at a large scale, and combined with active engagement of healthcare providers, as well as inspections.

With some exceptions, most healthcare professionals met by the visiting team had limited knowledge of the appropriate antibiotic use, AMR, IPC and AMS.

There is a health promotion department at the IPH. This department reaches the public through social media, the IPH website, leaflets, posters and other channels. However, to date, this department has not been involved in any activity to raise awareness of AMR or the prudent use of antibiotics.

European Antibiotic Awareness Day and World AMR Awareness Week are observed every year, mainly targeting health professionals. Some of these activities have gained media coverage and reached the general public. For example, for World AMR Awareness Week 2023 and with support from the WHO country office, a panel discussion attended by 169 participants was held in Skopje on 14 December 2023 under the theme 'Prevention of Antimicrobial Resistance Together.' The event was accredited by the Medical Chamber, the Pharmaceutical Chamber and the Veterinary Chamber of the RNM [18]. No reports on activities organised for European Antibiotic Awareness Day, i.e. 18 November 2023, were presented to the visiting team.

4.2.9 Marketing-related issues

All antibiotics are prescribed by generic name (rather than commercial product name) and the selection of antibiotics dispensed in pharmacies is based on price and availability. Both community and hospital pharmacies provided evidence for the prescription of antibiotics according to the active compound.

Pharmaceutical companies have direct access to healthcare professionals and pharmacists. Professional associations organise webinars and educational activities, sometimes with the financial support of pharmaceutical companies.

By law, financial support provided by companies to prescribers, such as participation in conferences, need to be declared and approved by the Ministry of Health. The Ministry has issued rules on the financial support received by healthcare professionals. According to the health professionals met, monitoring of adherence to the sponsorship rules used to be better enforced but seems now more relaxed.

There is a perception that due to the high cost of participation fees and travel, access to high-level educational activities is difficult unless sponsored by pharmaceutical companies. However, according to the 'Law on Health Protection', the professional development of the healthcare personnel should be covered through the public budget.

4.2.10 Conclusions on human health aspects of antimicrobial resistance

The high levels of multidrug-resistant pathogens isolated from inpatients together with the inadequate IPC programmes in healthcare facilities pose a significant threat to patient safety in North Macedonia. The situation is driven by various factors including the inappropriate use of broad-spectrum antibiotics in both the community and hospitals along with sub-optimal surveillance and prevention of HAIs.

More specifically, there is a lack of dedicated surveillance for AMR; often data collection does not include information on AST results for the isolated pathogens. Surveillance activities are limited to data collection and the knowledge and experience acquired through participating in different international surveillance networks (CAESAR, GLASS, ECDC networks) is not applied to the national and local levels. The implementation of an electronic surveillance system, based on the 'Moj Termin', will be a useful tool to support AMR surveillance and related activities. A dedicated AMR surveillance system at the national level, including definitions and specifications for data processing (i.e. surveillance methodology), is needed. AMR data collected at the local and national level should be used for trend analyses, stratified by healthcare setting (hospital-specific/primary care), geographical/administrative level (national, regional or local level) and AST profile. These analyses will provide the evidence for designing and implementing activities to prevent and control AMR. In addition, there is a lack of collaboration between disciplines (e.g. epidemiologists, microbiologists, clinicians, pharmacists, nurses) based on common goals and projects aiming at analysing and translating local and national AMR data into public health interventions.

In North Macedonia, AMC is being monitored using data from wholesales and, prescriptions from the healthcare providers in agreement with the HIF. The capacity to monitor AMC nationally has been enhanced by reporting national AMC to WHO since 2013, an integrated system is needed to compile and make sense of AMC data from the several, separate, non-standardised systems hosted in different institutions. Despite the existing national legislation banning the dispensation of antibiotics without prescription, the observed differences between AMC rates, calculated based on wholesale data and on prescription data, point at over-the-counter dispensation of antimicrobials in North Macedonia. Clinical pharmacists in the visited hospitals as well as community pharmacists are aware of the high AMC in the country and there is a need for increased education on the prescription of antimicrobials, dispensation of antimicrobials and antimicrobial use in general, as well as reporting, data collection, analysis and feedback on AMC.

This should be a priority as there is overuse and misuse of broad-spectrum antibiotics such as amoxicillin-clavulanic acid, third-generation cephalosporins, carbapenems, at all levels of the healthcare system. The visiting team was told that treatment guidelines were available either on the Ministry of Health webpage or at healthcare facilities but, during the visit, we found no confirmation that evidence-based guidelines for the management of patients were followed by doctors. Moreover, most of the doctors did not know about the existence of such guidelines. Additionally, diagnostic tests (blood cultures, rapid tests) to inform the use of targeted antimicrobial therapy are underused. There is also a lack of active ASP and AMS committees in the public hospitals to monitor antimicrobial use and compliance with the guidelines when they exist. All healthcare professionals prescribing antimicrobials require regular training on the appropriate use of antimicrobials according to the AWaRe classification. They also need to be aware and be continuously educated on the most recent evidence-based guidelines for the treatment of infections as well as for preoperative antibiotic prophylaxis. Prescription of antimicrobials should be audited regularly to give feedback to prescribers.

Moreover, there is no designated National Reference Laboratory with the capacity for second-line AST or confirmation of species identification as well as phenotypic and genomic AST, although the laboratories at the IPH and the IMP both have this capacity. Most of the laboratories in North Macedonia, including both IPH and IMP, participate in the CAESAR external quality assessment. Although both laboratories have the expertise in place to undertake quality bacteriology and AMR diagnostics, there were few clinical microbiology samples and underutilisation of clinical microbiology services for timely patient care and for AMR monitoring. The laboratory network in North Macedonia uses EUCAST breakpoints and related guidance for AST. These laboratories provide microbiology and AMR diagnostic services for both public hospitals and some private hospitals. The implementation of a web-based laboratory information management systems, which is currently unavailable, will provide real-time data-sharing capacity from the public health laboratories and IPH, which should improve the timeliness of reporting results. However, the data analysis capacity at the national level is lacking. Improving data access and capacity for data analysis will enhance the ability of the laboratories to alert and support AMR outbreak investigations.

The Rulebooks on the detailed criteria for the prevention and control of HAIs and IPC need to be updated and interventions urgently implemented by the IPC committees. The proper functioning of IPC committees was only noted at the visited private hospital and geriatric hospital. Considerable improvement of IPC practices is needed in the public hospitals as we observed: (i) limited knowledge of the HAI definitions and inappropriate surveillance of HAIs; (ii) lack of hand hygiene compliance surveillance and audits; (iii) no dedicated IPC staff in the public hospitals; (iv) inappropriate infrastructure and equipment (e.g. missing alcohol-hand rub bottles at point of care and missing disposable paper dispensers near sinks).

The current legislation on communicable diseases surveillance and related rulebooks are outdated and need to be urgently updated to include AMR with clear definitions. However, publication in the Official Gazette (assuming knowledge and application of these guidelines) does not guarantee that the legislation is understood and complied with. There is a lack of monitoring and evaluation activities to follow-up implementation of the activities and these need to be included in the legislation and within the responsibilities of all actors involved in AMR, AMC, HAIs and IPC.

In the field of education, compulsory educational programmes, focusing specifically on AMR, AMS and IPC and targeting future healthcare professionals, including nurses, should be established and promoted.

The limited awareness of the general public on the prudent use of antibiotics and, in general, AMR was flagged by many healthcare professionals, but it was also evident that, even among healthcare workers, there was a lack of knowledge of these topics. Only limited activities on the awareness of the prudent use of antibiotics targeting healthcare professionals have been organised during European Antibiotic Awareness Day and World AMR Awareness Week. Posters with key messages on AMR and the prudent use of antimicrobials were not seen by the visiting team in public areas, in pharmacies, healthcare settings or public health institutions. Limited resources were available to produce information leaflets and posters, as well as for their distribution or display in public spaces. There is also a need for behaviour change communication campaigns on the prudent use of antibiotics and AMR, with a systematic evaluation of the achievements related to behaviour change.

All antibiotics are prescribed by generic name and the selection of the antibiotic brand is made at the pharmacy, at the time of dispensation, based on price and availability, and this is a good practice. In addition, by law, all financial incentives that pharmaceutical companies may offer to healthcare professionals need to be declared and approved by the Ministry of Health. However, pharmaceutical companies have direct access to prescribers and the enforcement of this law should be strengthened.

4.3 Animal health, food safety and environmental aspects of antimicrobial resistance

4.3.1 Diagnostic laboratory services and reference laboratory services

The Faculty of Veterinary Medicine – Skopje (FVMS) is the officially designated reference laboratory for AMR in the animal health and food safety sector. The National Veterinary and Food Institute² is an organisational unit under FVMS composed of 12 laboratories accredited under ISO 17025, of which four cover AMR-related laboratory activities. Namely, the laboratory for microbiology of food and feed, the laboratory for molecular analysis of food and genetically modified organisms (GMOs), the laboratory for clinical microbiology and the laboratory for molecular diagnostics.

The laboratory for microbiology of food and feed is responsible for food safety microbiology analyses while the laboratory for clinical microbiology oversees animal health.

Both laboratories have established good collaboration with the EU Reference Laboratory on Antimicrobial Resistance (EURL-AR) and reference laboratories in EU Member States. They regularly participate in the EURL-AR proficiency testing schemes.

Laboratory capacity to undertake bacteriology analyses (isolation, pathogen identification and AST using phenotypic methods) is available at the laboratory for microbiology of food and feed and the laboratory for clinical microbiology. Molecular diagnostic capacity is available in the laboratory for molecular analysis of food and GMOs and the laboratory for molecular diagnostics, where there is the capacity and expertise to run real-time PCR (RT-PCR) on specific antimicrobial resistance genes (ARGs) to complement phenotypic AST.

The laboratory for microbiology of food and feed is the one performing surveillance for EU harmonised monitoring of certain zoonotic pathogens and indicator bacteria in animals and foods (Commission Implementing Decision (EU) 2020/1729 [19]), further described in the next section, using advised minimum inhibitory concentrations (MICs) methods.

Every laboratory is outfitted with standard equipment; all equipment is fully functional, regularly maintained and calibrated according to ISO 17025 requirements. Additionally, they all utilise the same laboratory information management system.

The laboratory for clinical microbiology is responsible for conducting essential diagnostic tests for companion and food-producing animals. The laboratory can perform culture of specimens, identification of microorganisms using MALDI-TOF or phenotypic tests, AST using CLSI and EUCAST standards for disc diffusion, and MIC determination using commercial panels. In addition, the laboratory has molecular diagnostic capabilities through RT-PCR and access to advanced technologies such as next-generation sequencing (NGS). However, due to the absence of official requests to perform NGS for AMR, this platform is only used for research purposes. During the visit, it was noted that the laboratory received more samples from companion animals than from farm animals. For companion animals, as mentioned to the visiting team, practising veterinarians often send samples for testing after failure of repeated treatment.

The laboratory for clinical microbiology extends its expertise and resources to support the microbiology department of the Institute of Public Health, and the Microbiology Institute for the confirmation of bacterial identification, particularly through applying MALDI-TOF technology.

The FVMS has an organised weekly sample collection and transport across the country. This collection and transport system is widely used by FVA for all monitoring programmes.

4.3.2 Monitoring antimicrobial resistance in animals and food

North Macedonia actively participates in the EU harmonised monitoring of AMR in certain zoonotic pathogens and indicator bacteria in certain animals and food, for zoonotic pathogens and indicator bacteria, as outlined in Commission Implementing Decision (EU) 2020/1729. Data have been reported to EFSA since 2018, indicating a commitment to providing AMR surveillance. Additionally, national legislation on monitoring AMR has been aligned with the relevant EU Decision to ensure consistency, and facilitate data sharing and comparison.

However, the first surveillance and monitoring campaign in 2021 only yielded 466 samples that were obtained from certain food-producing animal populations, including laying hens, broilers, cattle under one year of age and fattening pigs, and food categories, e.g. fresh meat from cattle pigs, broilers in retail. This limited number of samples led to only 108 relevant bacterial isolates being identified (e.g. *E. coli* and *Salmonella* spp.).

² Starting 1 March 2024, the Veterinary Institute, Food Institute and Institute for reproduction and biomedicine become the National institute for veterinary and food safety

Despite participation, the sampling coverage and number of tested isolates do not fully comply with EU requirements due to various factors, including budgetary constraints.

The sampling strategy does not adequately target the main food-producing animals, leading to a lack of proportional representation of animal populations in surveillance monitoring activities.

The low number of isolates obtained through current monitoring practices make it difficult to accurately assess AMR trends, and to identify emerging AMR patterns and effectively implement targeted interventions.

For pathogens from food-producing and companion animals, there is no systematic surveillance monitoring and the available information is scattered and limited to a few relevant point prevalence studies conducted by PhD/Master students or researchers. This lack of comprehensive data hinders the availability of timely and reliable information, which could aid informed decision-making regarding treatment options and general AMR management.

4.3.3 Monitoring the use of antimicrobials in animals

The FVA authorises VMPs and has a list of authorised VMPs available on its website³. The list of antimicrobials authorised for use in humans and sold to veterinarians in pharmacies to be used for animals was considered relatively small. The visiting team was informed that there were only two feed mills producing medicated feed. Prescription of antibiotics can only be done by a practising veterinarian, with 'physical' prescriptions to record the use of antimicrobials in animals. Antimicrobials can also be obtained directly from the herd veterinarian, requiring farmers to establish contracts with their own veterinarians for herd health oversight. Such contracts encompass VMPs.

Legal requirements for reporting data on imports and sales of VMPs by wholesalers, pharmacies and veterinary practices are in place. Since 2014, data on VMPs imported to North Macedonia for food-producing and companion animals have been reported to the World Organisation for Animal Health via the ANIMUSE platform, indicating a commitment to transparency and international collaboration. Furthermore, personnel handling the data demonstrate a good understanding of VMPs and their distribution, helping efforts to assess trends and patterns. However, there is a lack of a national template for semi-automatic data delivery from VMP stakeholders (wholesalers, pharmacies and veterinary practices), hindering the process and potentially leading to errors. Additionally, there is a deficiency in validation methods and semi-automatic tools for checking data completeness and accuracy, highlighting the absence of an established data quality management system (DQMS). Moreover, there is limited capacity to establish a collection system for data on the use of antimicrobials, as now mandated in the EU for the main food-producing species, indicating a gap in monitoring capabilities that could hinder effective antimicrobial stewardship efforts.

The FVA performs official controls, at a pre-defined frequency, but also risk-based controls of veterinarians, VMP stakeholders and farmers. Animal keepers cannot easily obtain human medicines, including antimicrobials. The surveillance data on AMC and antimicrobial sales and use are therefore believed to correctly reflect antimicrobial consumption/use from the human and animal sectors, respectively.

4.3.4 Activities to promote the reduced and/or prudent use of antimicrobials in animals

The veterinarians met by the visiting team were aware of AMR in general. The country's regulations mandating prescriptions for antimicrobials and other VMPs, along with robust record-keeping practices, closely align with previous EU legislation. Some veterinarians were also aware of the problems with 'overprescribing', over-the-counter sales and the possible animal safety risk due to the current AMR situation in North Macedonia. The requirement for farmers to have contracts with attending veterinarians, offering an option for an annual fee covering all services and medicines, fosters collaborative relationships and ensures regular veterinary visits. Veterinarians' services have been reported to be generally affordable for animal keepers.

Although the laboratories at the FVMS provide AST services for clinical samples using the disc diffusion method, the visiting team was informed that this option is not frequently used. The personnel of the FVMS mentioned that this may be due to logistical difficulties in referring samples to the FVMS, perceived long waiting times for obtaining results, and perceived high costs of AST by animal owners. Additionally, veterinarians and the FVA were not aware of any 'on-farm' testing methods (rapid test for mastitis, ready to use chromogenic media, etc.) that could help to overcome the logistical challenges involved in shipping samples to veterinary laboratories.

³ https://fva.gov.mk/images/2017_22_Список-ВМП.pdf

During the visit, the veterinarians treating large animals admitted being under pressure to use the most effective antimicrobials with the shortest withdrawal periods. They routinely prescribed broad-spectrum antibiotics e.g. third-generation cephalosporins for respiratory diseases in cattle and/or fluoroquinolones for mastitis in milking cows – both antibiotic classes are considered critically important antimicrobials (CIAs) for human health. The veterinarians met by the visiting team were not aware of the CIAs and the risks associated with using them as first-line treatment. They admitted to preferring empirical treatments with broad-spectrum antibiotics, including CIAs, as well as combinations of antimicrobials to ensure positive treatment outcomes and to avoid the risk of losing clients.

One of the farmers met by the visiting team used an intramammary herbal ointment based on essential oils for the treatment of non-severe cases of mastitis. His veterinarian explained that this was done to avoid the use of antimicrobials, although the motivation for such an approach, was to avoid the withdrawal period for milk. The same farmer explained that he dries off his cows without the use of antimicrobials, but by gradual reduction of milking and reduced feeding 70 days before the expected birth of the calves. This farmer also stated that he generally avoids problems with weaning diarrhoea of piglets by postponing weaning until they reach 35 days of age as well as good biosecurity practices. It must be noted that the farmers met by the visiting team kept a relatively small number of animals.

According to their veterinarians, the large commercial pig farms wean piglets at 22 to 28 days and use medicated feed to mitigate potential infections related to early weaning. None of the veterinarians met by the visiting team worked in such farms and therefore were not able to provide more details.

The FVA has outlined the plans to harmonise national legislation with current EU requirements on VMPs and medicated feed by the end of 2024. The visiting team did not identify, and it was not reported, that antimicrobials intended for use as growth and yield promoters (which are banned in the EU) were authorised as VMPs. Antimicrobials reserved for the treatment of humans (as set out in Regulation (EU) 2022/1255 [20]) were not authorised as VMPs. However, there were no controls in place to ensure that the human medicinal products containing such antimicrobials were not used in animals, in particular in companion animals.

The visit team was informed about recent infrastructure and biosecurity improvements in several medium and large-sized poultry farms, with the support provided by the FVA through projects funded by the Food and Agriculture Organization. The FVA demonstrated awareness of emerging challenges, particularly regarding hygiene and biosecurity on small farms, and is initiating proactive actions to address these issues. However, despite efforts by the FVA, many small farms still exhibit poor hygiene and biosecurity practices due to limited resources for infrastructure improvement.

For companion animals, it was reported that veterinarians may experience pressure by pets' owners to prescribe broad-spectrum antimicrobials, thus potentially contributing to the overuse or misuse of antimicrobials and fostering the development of AMR. Staff from the visited laboratory also mentioned that samples are often taken after prolonged treatment, resulting in a high percentage of multidrug- and pandrug-resistant isolates. This suboptimal testing approach hampers early detection of AMR and the implementation of interventions, thus exacerbating AMR challenges in the veterinary sector.

If they were implemented, activities to promote prudent use of antimicrobials and reduce unnecessary use of antimicrobials in animals (if they were implemented) would face the difficulty of reaching all the farms since, in North Macedonia, the farming sector is still characterised by many backyard farms. Nevertheless, the requirement for formal contracts between each farmer and a veterinarian overseeing the health of animals on the farm, the number of practising veterinarians being reported as adequate and the obligation to keep treatment records are assets that could be leveraged to increase the number of activities on the prudent antimicrobial use in animals.

4.3.5 Communication and awareness activities on antimicrobial resistance and the prudent use of antimicrobials in animals

The FVA has demonstrated proactive efforts by publishing guidelines, including those on the responsible use of antimicrobials, on its website. According to the FVA representatives, the guidelines have also been distributed at the time of their publication via the veterinary council, thus enhancing accessibility and dissemination of crucial information. However, the veterinarians met during the field visit were not aware of FVA's guidelines. This highlighted potential gaps in the dissemination and uptake of the guidelines. Additionally, FVA's AMR awareness-raising activities were put on hold in 2020 due to the COVID-19 pandemic, and there has been very limited subsequent communications.

In the past, prior to commencing the AMR monitoring activities, the FVA has conducted courses for official staff. According to FVA's representatives, the training included some general information on AMR, but mainly focused on the EU model for harmonised AMR monitoring.

Furthermore, continuing professional development (CPD) requirements for practising veterinarians ensure ongoing education on and awareness of AMR. Nevertheless, there appears to be a preference for training new clinicians in veterinary practices, with less emphasis on CPD of experienced practitioners. This approach may overlook the evolving nature of AMR and the need for ongoing skill enhancement.

The FVMS offers comprehensive undergraduate education, including elective modules addressing responsible antimicrobial use and AMR. Additionally, postgraduate specialisation in 'Food Safety and Security' covers relevant aspects of AMR. Nonetheless, the observed absence of common cooperation or modules for human and veterinary medicine students suggests a gap in fostering interdisciplinary collaboration which is essential for effectively addressing complex issues such as AMR.

Within the FVMS, PhD students are actively engaged in research on AMR, with collaboration extending to PhD students in human medicine, fostering interdisciplinary approaches. International student exchange programmes facilitate exposure to diverse perspectives on AMR. Student-led events, such as those targeting pet owners, demonstrate proactive efforts to raise awareness and engage the community on AMR-related issues.

It was reported that the 'Days of Veterinary Medicine', a conference organised by FVMS, attracts good attendance indicating interest and engagement with students and the professional community. The most recent conference in 2022 had a specific module on AMR.

4.3.6 Environmental aspects of antimicrobial resistance

The previous NAP (2019-2023) acknowledged the need for legislation to prevent environmental contamination with antimicrobials and establish safe disposal routes for expired and unused medicines. However, despite this recognition, there remain no safe routes for disposing unused and expired medicines, including antimicrobials, available to professional groups and the general public.

While there is ongoing work towards transposing and implementing the EU Water Framework Directive [21] and other relevant legislation, there is still a lack of regular monitoring of environmental contamination by antimicrobials, antimicrobial-resistant bacteria and ARGs. Without comprehensive monitoring, it is challenging to assess the extent of environmental contamination and effectively implement targeted interventions.

Individual studies targeting the environment are being conducted as part of research projects at the FVMS, indicating a recognition of the importance of understanding the environmental impact of antimicrobials and AMR. However, despite these research efforts, the visiting team noted lack of progress on the actions planned in the previous NAP, thus suggesting a disconnect between research findings and policy implementation.

4.3.7 Conclusions on veterinary and environmental aspects of antimicrobial resistance

The FVMS serves as the officially designated reference laboratories for AMR in the animal health and food safety sector, with accredited bacteriology laboratories and molecular diagnostic capabilities.

North Macedonia actively participates in EU harmonised monitoring of animals and food for zoonotic pathogens and indicator bacteria. The sampling coverage and the number of tested isolates may not yet be fully compliant with the EU requirements, but there is a good disposition to investigate the issue and scale up efforts.

The country lacks a comprehensive national surveillance system for monitoring AMR in veterinary pathogens, leading to scattered and limited information on the AMR levels of such pathogens.

While in the past, some efforts were made to spread awareness of AMR and promote reduced and prudent use of antimicrobials in animals, this effort had a very limited effect. Veterinarians were pressured by the animal keepers to provide effective treatment and choose antimicrobials with a minimal withdrawal period. Broad-spectrum antimicrobials, including CIAs, were routinely prescribed. There were also additional challenges such as the large number of backyard farms with low biosecurity standards and the smallest ones being outside of official controls.

Communication and awareness efforts regarding AMR and the responsible use of antimicrobials in animals were hampered by gaps in the dissemination and adoption of guidelines, as well as the discontinuation of awareness-raising activities, which was further prolonged during the COVID-19 pandemic.

Despite acknowledging the need for legislation to prevent environmental contamination with antimicrobials, North Macedonia faces challenges in establishing safe disposal routes for expired and unused medicines, including antimicrobials, as well as in effective monitoring of environmental contamination.

5. Conclusions

Conclusions concerning human health

The recently appointed MCCAMR should urgently update and implement the NAP on AMR in a One Health approach utilising adequate resources ensured by political endorsement.

National legislation needs to be updated and aligned with EU legislation, while evidence-based clinical guidelines and protocols should be developed for managing patient infections in both the community and hospitals. Emphasis should also be given to recommendations for surgical prophylaxis. National-level surveillance of AMR and HAIs must be established using the appropriate case definitions.

To support surveillance, the designation of a laboratory as a national reference laboratory for AMR is essential. The microbiology laboratory at the IPH can serve as a National Reference Laboratory but would need to be formally designated and be provided with dedicated financial support for this function. There is a good informal relationship between microbiologists and clinicians and a laboratory information management system is under implementation in the country but is not yet available to all laboratories which makes timely reporting of results to clinicians difficult. In addition, there is underutilisation of clinical microbiology services in hospitals and a low frequency of testing, including AST, that results in suboptimal patient management and undermines the representativeness of surveillance data.

North Macedonia actively engages in European and international AMR surveillance networks such as CAESAR, GLASS, and ECDC networks, contributing to the global efforts to monitor AMR. While most laboratories are part of these networks and report AMR data to the IPH following the CAESAR protocol, the current reporting system is paper-based, resulting in limited data analyses and integration with the communicable disease surveillance system.

Although the IPH compiles available AMR surveillance data into reports, there is a need for more advanced analyses and feedback mechanisms. This includes providing feedback to clinicians and other stakeholders, including decision-makers, to inform the design and implementation of targeted public health interventions. Enhanced data analyses and feedback loops are crucial for effectively combating AMR and reducing its impact on public health in North Macedonia.

Currently, available AMC data are based on the prescriptions from healthcare providers having an agreement with the HIF as well as the wholesale data provided by the Macedonian Agency for Medicines and Medical Devices. There is no system in place to monitor AMC data from both hospitals and primary care. Additionally, despite the existing legislation banning over-the-counter dispensation of antibiotics without a prescription, there is evidence that antibiotics are sold without a prescription. Urgent implementation of integrated AMC monitoring systems in hospitals and in primary care is needed.

There is no national ASP. Guidelines for the diagnosis and treatment of infectious diseases are either unavailable or, if available, little known or used (guidelines for surgical prophylaxis) by medical doctors. In all sectors of human medicine, this results in misuse or overuse of antimicrobials, especially of broad-spectrum and last-line antimicrobials. A good example of a functioning ASP was observed in the private hospital visited and similar initiatives could be extended to public hospitals and other healthcare facilities.

IPC committees were in place in all visited hospitals. The 2009 Rulebook for HAI control and IPC is considered outdated. The proper functioning of IPC committees was noted for several of the visited hospitals. However, based on the observations of the visiting team, there are several key issues that need to be addressed to improve IPC including (i) limited knowledge of the HAI definitions and inappropriate surveillance of HAIs; (ii) lack of hand hygiene compliance surveillance and audits; (iii) absence of dedicated IPC staff in the public hospitals; (iv) inappropriate infrastructure and equipment necessary for effective IPC. In the visited hospitals, adherence to good hospital IPC practices was insufficient, suggesting the need of behaviour change interventions.

Besides participation in the annual European Antibiotic Awareness Day and World AMR Awareness Week, for which activities mainly targeted health professionals, the visiting team was not informed about other awareness raising activities. There is insufficient knowledge of appropriate use of antibiotics and IPC within the general public and among healthcare practitioners and hospital managers. There is a need to assess the main drivers (behaviours, perceptions, cultural beliefs) related to overuse and misuse of antimicrobials to plan and implement behaviour change interventions.

Conclusions concerning animal health

North Macedonia has designated the FVMS as the reference laboratories for AMR in the animal health and food safety sector. The laboratories are accredited for bacteriology testing, and there are quality assurance measures in place. However, there are challenges in reporting AMR data according to EU harmonised protocols due to the high cost of MIC testing panels. Also, the rare clinical samples from animals sent to the FVMS hampers the capacity to measure the spread of AMR in farms and the food industry for key priority zoonotic and/or commensal bacteria.

Despite active participation in EU harmonised monitoring efforts for food-producing animals and food, the sampling coverage and the number of tested isolates may not yet be fully compliant with the EU requirements, but there is a good disposition to investigate the issue and scale up efforts. There is also a lack of a comprehensive national surveillance system for monitoring AMR in veterinary pathogens, limiting the availability of timely and reliable information for informed clinical decision-making for treatment of infected animals.

While legal requirements for reporting data on imports and sales of VMPs are in place, there are deficiencies in data validation methods and tools for checking data completeness and accuracy. Additionally, there is limited capacity to establish a collection system for data on the use of antimicrobials, indicating a gap in monitoring capabilities.

North Macedonia has regulations in place for prescriptions of antimicrobials and other VMPs, along with robust record-keeping practices. However, there are challenges related to logistical difficulties in AST of pathogens from clinical samples and pressure on veterinarians to prioritise effective treatment, potentially leading to the overuse of antimicrobials.

While proactive efforts have been made by the FVA in publishing guidelines and conducting courses for official staff, there are gaps in the dissemination and uptake of crucial information, as some veterinarians met by the visiting team were not aware of FVA guidelines. Additionally, there is a need for ongoing education and awareness-raising activities on AMR for practising veterinarians.

North Macedonia has recognised the need for legislation to prevent environmental contamination with antimicrobials and establish safe disposal routes for expired and unused medicines, including antimicrobials. However, there are challenges in implementing these measures, including a lack of safe routes for disposing of unused and expired medicines and a lack of regular monitoring of environmental contamination.

The commitment demonstrated by relevant stakeholders in North Macedonia's human health, food production, and veterinary sectors marks a promising starting point in the effort to effectively manage AMR and advocate for the judicious use of antimicrobials in the country. Several challenges persist in monitoring AMR from a comprehensive One Health perspective and in establishing robust prevention and control measures across all sectors, particularly in the human health and environmental sectors. During the country visit, the collaborative engagement between the ECDC/EFSA/DG SANTE visiting team and national authorities, service providers, and stakeholders responsible for One Health AMR-related activities in the country was notable. This collaboration bodes well for future endeavours aimed at leveraging achievements and enhancing AMR control efforts across all sectors.

6. Considerations for future actions

The options for future actions provided below have been identified by the visiting team of experts from ECDC, EFSA, DG SANTE, Epiconcept and Integrated Quality Laboratory Services and may be useful for the relevant competent authorities and stakeholders to support North Macedonia in further strengthening the development and implementation of a One Health AMR Plan and immediate and long-term sectoral actions.

6.1 Governance and One Health aspects of antimicrobial resistance

Intersectoral collaboration and NAP

- Reinforce the role of the MCCAMR. The MCCAMR should have a clear Terms of Reference with specific roles, responsibilities and dedicated time and budget. The MCCAMR should meet regularly, provide minutes of its meetings, and involve all actors working with or having an interest in AMR, integrating all good initiatives and projects and taking advantage of existing technical expertise in IPC and ASP (e.g. from the academic, public and private sectors).
- Develop and implement the NAP on AMR with specific timelines, allocating sufficient budget to all specified activities, but without postponing actions that would delay completion of the NAP.
- Include measurable indicators and targets into the NAP, considering the Council recommendation on stepping up actions to combat antimicrobial resistance in a One Health approach (2023/C 220/01).
- Continue the collaboration in a One Health perspective, with enhanced co-operation between human and animal health/food safety and involving the environmental sector.
- Provide sustained national funding for both MCCAMR activities and implementation of the updated NAP on AMR as well as the political support needed to accomplish MCCAMR and NAP tasks.
- The NAP on AMR should define the goals and objectives based on surveillance and benchmarking and include a regular evaluation of its effectiveness and the lessons learned.

6.2 Human health aspects of antimicrobial resistance

Priority and key actions

- Urgently address the current rapid dissemination of carbapenem-resistant gram-negative bacteria in hospitals and healthcare settings in the country.
- Strengthen IPC in hospitals, starting with ICUs, by ensuring appropriate human and financial resources for sustainable implementation of IPC interventions.
- Introduce protocols (e.g. management of patients with infections) and clinical guidelines for appropriate use of antibiotics.
- Initiate surveillance on AMR, AMC, HAIs and IPC practices according to EU standards.
- Share results of AMR, AMC, HAI surveillance data analysis and IPC indicators with hospital managers and all other relevant stakeholders to engage them in the planning and execution of interventions.
- Invest in professional development to train future AMR champions.
- Enforce efforts to raise awareness of AMR and prudent use of antibiotics through national campaigns addressing the current expectation of antibiotics by the public and consequent pressures on doctors.

Diagnostic laboratory services and reference laboratory services

- Designate a National Reference Laboratory on AMR with clear Terms of Reference and a dedicated budget focused on second-line and confirmatory testing of bacterial and fungal pathogens and AST.
- Increase the demand for microbiological testing by issuing diagnostic stewardship guidance on indications for sampling, appropriate sampling procedures as well as training of the healthcare staff accordingly.
- Improve access to timely clinical microbiology services by establishing laboratory information management systems in clinical laboratories and immediate reporting of critical results to clinicians.
- Improve feedback and reporting to providers by strengthening communication and collaboration between microbiologists and clinicians and providing feedback from the National Reference Laboratory on AMR to clinical microbiology laboratories.

Organised multidisciplinary collaboration at the local level

- Strengthen the collaboration among different stakeholders from universities, healthcare facilities and the public health institute by sharing best practice, expertise, and information to promote mutual learning and improvement.
- Implement systematic methods for the collection, reporting, and analysis of available data on AMR and AMC at all levels, enhancing decision-making and resource allocation.
- Establish clear channels for communication and foster a bidirectional flow of information to facilitate effective collaboration and responsiveness to emerging challenges related to AMR.
- Coordinate interventions across stakeholders to maximise impact and avoid duplication of efforts, promoting efficiency and synergy in addressing AMR effectively.

Monitoring antimicrobial resistance in the human sector

- Update the Law on Protection from Communicable Diseases to include AMR as a specific health issue requiring mandatory surveillance. Update the Rulebook on case definitions to include the most recent definitions on HAIs and any additional pathogen with high levels of antimicrobial resistance in the notifiable pathogen list.
- Establish a national AMR surveillance, including AST data from notifiable pathogens from all available clinical specimens, with clear objectives and definitions (including for alerts) and a detailed description of procedures (surveillance methodology).
- Perform analysis of AMR data at least quarterly and providing feedback to data providers.
- Publish national reports on AMR (at least annually).
- Continue participation in European and international surveillance networks such as CAESAR and GLASS.

Monitoring of AMC in the human sector

- Implement a national AMC monitoring system gathering data from all hospitals and primary care practices, and not only those having an agreement with HIF.
- Ensure that hospital pharmacy information systems allow that AMC data can be easily extracted, used to produce reports, provide feedback and linked to other hospital information systems.
- Provide AMC data in DDD per 100 patient-days (or occupied bed-days) for all individual hospitals, disaggregated by department or area.
- Enforce national legislation banning over-the-counter dispensation of antimicrobials without medical prescription.
- Strengthen professional capacity regarding AMC, dispensation of antimicrobials, reporting, data collection, analysis and feedback.

AMS and treatment guidelines in the human sector

- Develop and adopt national evidence-based comprehensive protocols for the management of infections, such as sepsis protocol, incorporating guidelines for when and how to take clinical samples tailored to specific clinical scenarios with less emphasis on the use of cephalosporins and other broad-spectrum antibiotics.
- Review and ensure accessibility of existing guidelines on diagnosis and treatment, making them readily available to healthcare professionals for reference and implementation.
- Establish AMS committees within healthcare facilities to oversee and guide antimicrobial prescribing practices. Appoint at least one dedicated infectious diseases physician per 500 beds and with full-time AMS duties, such as addressing the empirical use of last-resort antibiotics (especially carbapenems) to ensure that:
 - Samples are taken before treatment is started,
 - Empiric prescribing is reviewed by an infectious diseases specialist,
 - A review of empiric treatment is performed within 72 hours and de-escalation undertaken as often as possible.
- Increase audits of antibiotic prescribing in hospitals to review the proportion of treatments started without the appropriate indication, prolonged surgical prophylaxis, etc.
- Provide managerial support to hospital/clinic administrations for ASPs and allocate dedicated funding to sustain AMS efforts effectively.
- Implement robust monitoring and evaluation mechanisms for AMS indicators, including AMC and adherence to guidelines, to assess the impact and effectiveness of AMS initiatives.
- Develop hospital-specific protocols to optimise the management of patients with infections by integrating appropriate diagnostic tools into clinical decision-making processes.
- Facilitate regular feedback loops to prescribers on their antibiotic prescribing patterns, accompanied by incentives for compliance with guidelines and appropriate prescribing practices, while considering potential sanctions for non-compliance.

- Institute a structured training programme for medical doctors focused on appropriate antibiotic prescribing practices, integrating AMS-related training into the continuous professional education agendas of relevant professional societies to ensure ongoing skill development and awareness.
- Increase the availability of and promote prescription of narrow-spectrum antibiotics. In the community, it is important that narrow-spectrum antibiotics such as amoxicillin, flucloxacillin and first-generation cephalosporins become more widely available and are the first-line treatment of bacterial respiratory infections where appropriate and when no risk factors are present.

Infection prevention and control

- Implement a national IPC programme to be applied in hospitals and other healthcare facilities, including SOPs, training and evaluation, and with dedicated staff and budget, i.e. at least one full-time IPC nurse for less or equal to 250 beds.
- Monitor IPC practices with regular audits and feedback:
 - Strengthening hand hygiene monitoring.
 - Promoting use of alcohol-based hand rub for hand disinfection and ensure the availability of alcohol-based hand rub at the point of patient care.
 - Monitoring infections associated with central venous- and urinary catheters.
- Provide regular IPC training for healthcare staff in all hospitals and other healthcare facilities.
- Invest in professional development to train future IPC healthcare professionals. IPC training with certification, including hands-on training and career pathways needs to be established.
- Establish national surveillance of HAIs.
 - Consider implementing systematic screening of patients, at admission and at regular intervals, in hospitals/regions experiencing outbreaks or endemicity of highly drug-resistant *Acinetobacter baumannii* and carbapenem-resistant Enterobacterales.

AMR and IPC education

- Enhance investment in a comprehensive professional development plan aimed at training future healthcare professionals. This includes integrating modules on IPC and AMS, and more generally AMR, into the undergraduate curricula of medical, nursing schools, and colleges of pharmacology.
- Integrate AMS- and IPC-focused training into the core priorities of continuous professional education provided by professional societies.

Public information and behavioural change interventions for AMR

- Assess the main drivers of AMR and AMC in the country to inform a behaviour change intervention.
- Plan a long-term behaviour change campaign by involving all actors to raise awareness of the general public (continuous public information through media, posters, European Antibiotic Awareness Day, World AMR Awareness Week) and of healthcare providers about AMR, prudent use of antibiotics, hand hygiene and prevention of infectious diseases.
- Consider using the materials developed by ECDC for European Antibiotic Awareness Day that would be useful with a translation in Macedonian and Albanian (see Annex 2) including communication toolkits to promote prudent antibiotic use aimed at: (i) primary care prescribers; (ii) professionals in hospitals and other healthcare settings; (iii) those self-medicating with antibiotics; (iv) the general public; and (v) for engaging in social media activities promoting prudent antibiotic use.
- Consider engaging pharmacies, the IPH and behaviour change specialists in planning and evaluating national awareness campaigns on AMR and prudent use of antibiotics.
- Regularly evaluate the impact of the implemented awareness campaigns via surveys.
- Establish interactions and collaboration with communication staff in professional organisations, to enhance outreach to professionals across the country directly.

Marketing-related issues

- Continue good practice on using the generic name for antimicrobials in prescriptions.
- Reinforce best practice and ethical principles on sponsorship of activities and access of pharmaceutical companies to healthcare providers.

6.3 Animal health and food safety aspects of AMR

Diagnostic laboratory services and reference laboratory services

- Increase sampling, microbiological testing and AST for AMR monitoring and from clinical samples.

Monitoring of AMR in animal health and the food sector

- Continue with the implementation of EU harmonised AMR monitoring in food-producing animals and food by a step-by-step approach:
 - Animal species: consider starting with one species based on the national production (e.g. poultry or cattle) and adding a second species in subsequent years, or rotate species every year.
 - Bacterial species: consider current sampling available (e.g. as *Salmonella* control plan is in place, the monitoring may start by testing for susceptibility to antimicrobials of *Salmonella* spp. isolates; or if sampling for microbiological criteria is in place, the monitoring may start from AST of the isolates from those samples); or consider starting from *E. coli* as general indicator since sampling intestinal material at slaughter level would be efficient (isolation from all species, samples can easily be collected by slaughter inspectors).
 - Progressively implement WGS to align with the EU requirements.
- Consider developing national surveillance of veterinary pathogens of clinical importance:
 - Identify pertinent pathogens present in major food-producing animal species and implement robust sampling and testing strategies to bolster surveillance efforts.
 - Prioritise AST incorporating antibiotic panels that accurately reflect antibiotics commonly used in the country in both animals and humans, thereby augmenting the capacity to inform clinicians about the best choice of antimicrobials when treating infections.
 - Sustain initiatives aimed at promoting point prevalence research surveys across various sectors of animal farming and companion animal care, to gain comprehensive insights into AMR prevalence.
 - Strengthen AST of veterinary pathogens, with a particular emphasis on diseases or conditions of significant interest to veterinarians, such as assessing antimicrobial susceptibility of pathogens responsible for mastitis in cattle, to better understand prevalent AMR patterns.
 - Utilise the findings from research and surveillance activities to inform evidence-based policymaking and to guide ongoing monitoring efforts for enhanced AMR management.

Monitoring of sales and use of antimicrobials in animals

- Explore the possibility of developing a country-specific system for collecting antimicrobial sales data, with a long-term goal of establishing a comprehensive data collection mechanism for antimicrobial use. This could involve:
 - Analyse the distribution flow of antimicrobial VMPs to understand their usage patterns.
 - Create a national reporting template to streamline the data reporting process for stakeholders.
 - Implement a DQMS to ensure the accuracy and reliability of the collected data.
 - Utilise documents that are publicly available from the European Medicines Agency (EMA) website to align with EU standards and practices.
 - Adopt the Population Correction Unit (PCU) developed by the EMA to adjust antimicrobial sales data based on the country's animal population, providing a more accurate representation of antimicrobial usage.
- Leverage the collected data to inform evidence-based policymaking and to design targeted interventions aimed at promoting responsible antimicrobial use in animals.

Activities to promote the reduced and/or prudent use of antimicrobials in animals

- Continue the collaboration between the FVA and FVMS on biosecurity at small farms.
- Explore strategies to incentivise the systematic use of diagnostic tests, including on-farm testing of milk samples, and AST to enhance prescribing practices.
- Consider: i) developing measures to promote reduced use of antimicrobials and ii) phasing out the systematic use of CIAs, considering both incentives and regulatory actions.

Education and communication

- Consider resuming training programmes for official veterinarians focusing on AMR awareness and the responsible use of antimicrobials.
- Consider targeted AMR awareness campaigns targeting veterinarians and animal keepers, including pet owners, to promote responsible use of antimicrobials.
- Consider how to distribute and promote existing treatment guidelines to ensure their accessibility and adoption by veterinary practitioners.
- Consider how to incorporate the findings from cumulative AST statistics conducted during research and surveillance activities into the development or update of treatment guidelines, reflecting the current AMR prevalence in the country.
- Establish regular One Health collaboration initiatives between students of human and veterinary medicine, such as shared modules, to foster interdisciplinary understanding and cooperation on AMR-related issues.

6.4 Environmental aspects of AMR

- Prioritise establishing safe disposal mechanisms for expired and unused medicines, including antimicrobials, to effectively mitigate environmental contamination risks.
- Maintain efforts towards harmonising national legislation with EU legislation, such as the Water Framework Directive, and initiate a comprehensive sampling programme for antimicrobial substances, including those listed in the Watch List under the WFD, to ensure compliance with EU legislation and safeguard the environment.
- Explore additional options for monitoring AMR and AMR genes in the environment, to bridge existing knowledge gaps and effectively mitigate environmental contamination risks.

References

1. The Burden of Bacterial Antimicrobial Resistance in the WHO European region in 2019: a cross-country systematic analysis. Mestrovic, Tomislav et al. *The Lancet Public Health*, Volume 7, Issue 11, e897 - e913. [https://doi.org/10.1016/S2468-2667\(22\)00225-0](https://doi.org/10.1016/S2468-2667(22)00225-0)
2. European Centre for Disease Prevention and Control (ECDC). Assessing the health burden of infections with antibiotic-resistant bacteria in the EU/EEA, 2016-2020. Stockholm: ECDC; 2022. Available at: <https://www.ecdc.europa.eu/sites/default/files/documents/Health-burden-infections-antibiotic-resistant-bacteria.pdf>
3. Jonas, Olga B.; Irwin, Alec; Berthe, Franck Cesar Jean; Le Gall, Francois G.; Marquez, Patricio V. Drug-resistant infections: a threat to our economic future (Vol. 2): final report (English). HNP/Agriculture Global Antimicrobial Resistance Initiative Washington, D.C: World Bank Group. Available at: <http://documents.worldbank.org/curated/en/323311493396993758/final-report>. <https://www.worldbank.org/en/topic/health/publication/drug-resistant-infections-a-threat-to-our-economic-future>
4. World Health Organization (WHO) Global action plan on antimicrobial resistance. Geneva: WHO: 2015. Available at: <https://www.who.int/publications/i/item/9789241509763>
5. European Centre for Disease Prevention and Control (ECDC). Amended ECDC Strategy 2021–2027. Stockholm: ECDC; 2023 Available at: [Amended ECDC Strategy 2021-2027](#)
6. European Centre for Disease Prevention and Control (ECDC). Meeting report: Regional workshop on a 'One-Health' approach to antimicrobial resistance in EU pre-accession countries. Stockholm: ECDC; 2019. Available at: <https://www.ecdc.europa.eu/sites/default/files/documents/antimicrobial-resistance-one-health-approach-EU-preaccession-countries.pdf>
7. European Centre for Disease Prevention and Control (ECDC). Assessment Tool for Joint 'One-Health' Country Visits in relation to Antimicrobial Resistance. ECDC: Stockholm, 2021. Available at: [One Health assessment tool for country visits relating to AMR](#)
8. European Centre for Disease Prevention and Control (ECDC) and World Health Organization (WHO). Antimicrobial resistance surveillance in Europe 2023 - 2021 data. Stockholm; 2023. Available at: [Antimicrobial resistance surveillance in Europe 2023 - 2021 data.pdf](#)
9. World Health Organization (WHO). Review of antibiotics in National Medicines Selection Lists in Eastern Europe and Central Asia. Copenhagen: WHO Regional Office for Europe; 2023. Licence: CC BY-NC-SA 3.0 IGO. Available at: <https://www.who.int/north-macedonia/publications/i/item/9789289058582>
10. World Health Organization (WHO). Evidence brief for policy. Promoting appropriate use of antibiotics in hospitals to contain antibiotic resistance in North Macedonia. Copenhagen: WHO Regional Office for Europe; 2020. Available at: [WHO-EURO-2020-5543-45308-64849-eng.pdf](#)
11. World Health Organization (WHO). Antimicrobials supplied in community pharmacies in eastern Europe and central Asia in the early phases of the COVID-19 pandemic. Copenhagen: WHO Regional Office for Europe; 2022. Licence: CC BY-NC-SA 3.0 IGO. Available at: <https://www.who.int/europe/publications/i/item/9789289058056>.
12. Singh-Phulgenda S, Antoniou P, Wong DLF, Iwamoto K, Kandelaki K. Knowledge, Attitudes and Behaviors on Antimicrobial Resistance among General Public across 14 Member States in the WHO European region: Results from a cross-sectional survey. *Front Public Health*. 2023 Nov 23;11:1274818. doi: 10.3389/fpubh.2023.1274818. PMID: 38074764; PMCID: PMC10704021. Available at: [Knowledge, attitudes and behaviors on antimicrobial resistance among general public across 14 member states in the WHO European region: results from a cross-sectional survey - PubMed](#)
13. European Commission (EC). 2022. Special Eurobarometer 522 'Antimicrobial resistance'. Available at: <https://europa.eu/eurobarometer/surveys/detail/2632>
14. European Commission (EC). Commission implementing decision of 8 August 2012 amending Decision 2002/253/EC laying down case definitions for reporting communicable diseases to the Community network under Decision No 2119/98/EC of the European Parliament and of the Council (notified under document C (2012) 5538) (2012/506/EU). Available at: <https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32012D0506>
15. World Health Organization (WHO). GLASS methodology for surveillance of national antimicrobial consumption. Geneva: World Health Organization; 2020. Licence: CC BY-NC-SA 3.0 IGO. Available at: [9789240012639-eng.pdf](#)
16. World Health Organization (WHO). The WHO AWaRe (Access, Watch, Reserve) Antibiotic Book. Geneva: World Health Organization; 2022. License: CC BY-NC-SA 3.0 IGO. Available at: [9789240062382-eng.pdf](#)
17. Ivanovska V, Angelovska B, van Dijk L, Zdravkovska M, Leufkens HG, Mantel-Teeuwisse AK. Change in parental knowledge, attitudes and practice of antibiotic use after a national intervention programme. *European Journal of Public Health*. 2018 Aug 1;28(4):724-729. doi: 10.1093/eurpub/ckx240. PMID: 29325065. [Change in parental knowledge, attitudes and practice of antibiotic use after a national intervention programme - PubMed](#)
18. BIOM report: Support for observation of the World Antimicrobial Awareness Week (WAAW) and the use of the immunization. Panel discussion "Preventing antimicrobial resistance together", Skopje, 14 December 2023
19. European Commission (EC). Commission Implementing Decision (EU) 2020/1729 of 17 November 2020 on the monitoring and reporting of antimicrobial resistance in zoonotic and commensal bacteria and repealing Implementing Decision 2013/652/EU (notified under document C (2020) 7894); OJ L 387, 19.11.2020, p. 8–21. Available at: [Implementing decision - 2020/1729 - EN - EUR-Lex](#)
20. European Commission (EC). Commission Implementing Regulation (EU) 2022/1255 of 19 July 2022 designating antimicrobials or groups of antimicrobials reserved for treatment of certain infections in humans, in accordance with Regulation (EU) 2019/6 of the European Parliament and of the Council. *OJ L 191*, 20.7.2022, p. 58–60. Available at: [Implementing regulation - 2022/1255 - EN - EUR-Lex](#)

21. European Parliament. Directive 2000/60/EC of the European Parliament and of the Council of 23 October 2000 establishing a framework for Community action in the field of water policy. *OJ L 327, 22.12.2000, p. 1–73*. Available at: <http://data.europa.eu/eli/dir/2000/60/oj>

Annex 1. Agenda of the country visit

| DAY 1: Monday 29 January 2024 | | |
|-------------------------------|--|------------------------------------|
| 08:30 – 09:15 (45 min) | <p>Opening meeting with national authorities and stakeholder</p> <ul style="list-style-type: none"> - Ministry of Health - Ministry of Agriculture Forestry and Water Economy - Ministry of Environment and Physical Planning - Director of the Food and Veterinary Agency - Director of the Institute of Public Health - Proxy Director of Pharmacy department/Advisor to the Director of the National Health Insurance Found - Director of the Agency for Drug and Medical Devices - All members of the Multi-sectorial Commission for Control of Antimicrobial Resistance (MCCAMR) - WHO CO Head of Office - <p>Round table short presentation of participants</p> <p>Presentation from ECDC, EFSA and DG SANTE on the objectives of the visit, expected outputs and outcomes, and the One Health concept</p> | Location: Hotel Holiday Inn |
| 09:15 – 12:45 (3.5 hours) | <p>Meeting with the Multi-sectorial Commission for Control of Antimicrobial resistance (MCCAMR) (ECDC, EFSA and DG SANTE Team)</p> <p>Governance, surveillance and One Health aspect of AMR</p> <p>Objective: gather information on the current situation of AMR governance and AMR surveillance strategies in North Macedonia</p> <p>Presentations:</p> <ul style="list-style-type: none"> • National AMR strategy and its implementation in North Macedonia: current policy and legislation in North Macedonia • Monitoring of AM use/consumption in human health • Monitoring AMR in human health in North Macedonia • Monitoring of AM sales/use in animal health sector • Monitoring AMR in animals and foods in North Macedonia, • Electronic surveillance of AMR • North Macedonia Laboratory capacity in Human and animal Health • Antibiotic awareness activities <p>Q&A session/Discussions on:</p> <ul style="list-style-type: none"> - Inter-sectoral coordination mechanism (indicators in section 1.1 of ECDC Assessment Tool) - National Action Plan (indicators in section 1.2) - Organized multidisciplinary collaboration at local level (indicators in section 2) - Monitoring of AMR (indicator 4) and antimicrobial consumption (indicators in section 5) - Clinical diagnostic and reference laboratory services (indicators in section 3) - Public information and behavioural change interventions related to AMR (indicators in section 9) | Location: same as above |
| 11:00 – 11:15 Coffee break | | |
| + group photo | | |
| 12:45– 13:45 | Lunch break | |
| 13:45 - 14:45 | Meeting with representatives of the Ministry of Environment, Ministry of Agriculture, Food and Veterinary Agency on Environmental aspects of AMR | Location: same as above |

| DAY 1: Monday 29 January 2024 | | |
|---|---|---|
| (1 hour) | <p>Presentation The environmental aspect of AMR and surveillance of AMR in the environment (main GAPs identified and plans)</p> <p>Discussion on:</p> <ul style="list-style-type: none"> - Environmental surveillance of AMR and residues of antimicrobials - EU harmonized monitoring of Watch list substances under the Water Framework Directive⁴ - Role of environment on the spread of AMR throughout the food chain and possible risk mitigations measures - Policies for disposal of unused and expired medicines | |
| Separate parallel meetings | | |
| 14:45 – 16:15 (1.5 hour) <i>Same location but different rooms</i> | ECDC team | DG SANTE and EFSA team |
| | <p>AMR in the human health sector – antimicrobial stewardship and IPC</p> <p>Presentations</p> <ul style="list-style-type: none"> - Antimicrobial Stewardship and Infection Prevention and Control (IPC) in North Macedonia - Education on AMR/IPC in curriculum of health professionals - <p>Discussions on:</p> <ul style="list-style-type: none"> - Antimicrobial stewardship and treatment guidelines (indicator 6), - Infection prevention and control (IPC) (indicator 7) - AMR and IPC education (indicators in section 8) - Public information and behavioural change interventions related to AMR (indicators in section 9) | <p>AMR in the animal and food production sectors</p> <p>Presentations:</p> <ul style="list-style-type: none"> - Overview of the farming sector structuration - Veterinary model for veterinary care for food-producing animals and companion animals, including sales mechanism <p>Discussions on:</p> <ul style="list-style-type: none"> - initiatives to promote prudent use - organization of official controls on the use of VMPs - the sales mechanism for AB on farming - model for veterinary care for food-producing animals and companion animals |
| 16:15 – 16:30 | Coffee break | |
| 16:30 – 17:30 (1 hour) <i>Same location but different rooms</i> | ECDC team | DG SANTE and EFSA team |
| | <p>Meeting with professional associations representatives and heads of chambers</p> <p>Presentation:</p> <ul style="list-style-type: none"> - Representatives of North Macedonia Medical Association / Medical Chamber, - Macedonian Microbiology Society, - The Association of General Practice/Family Medicine (AGP/FM) - Macedonian Society of Anaesthesia & Intensive Care - Society of Infection Prevention & Control - North Macedonian Pharmacy Association - Macedonian Association of Hospital pharmacies - Macedonian Pharmaceutical Society - North Macedonian Society for Infectious Diseases - Society of Epidemiologists of North Macedonia | <p>Meeting with professional associations representatives and heads of chambers</p> <p>Discussion with veterinary professional organization(s), pharmacist, wholesalers of VMPs, veterinary chamber</p> <ul style="list-style-type: none"> - Veterinary Chamber of North Macedonia - Representative of sectorial branch - Veterinary practice and Veterinary Wholesale Pharmacies <p>Short oral presentation by the associations on the farming sectors they cover, the memberships levels and activities undertaken by the associations on AMR</p> |

⁴ Directive 2000/60/EC of the European Parliament and of the Council establishing a framework for community action in the field of water policy, OJ L 327, 22.12.2000, p. 1.

| DAY 1: Monday 29 January 2024 | | | | | |
|--------------------------------|--|---|-------------------------------|--|------------------------------------|
| | | Discussion on educational programmes and awareness campaigns, treatment guidelines, strategies and initiatives to reduce antimicrobial consumption/antibiotic stewardship. | | | |
| DAY 2: Tuesday 30 January 2024 | | | | | |
| ECDC team | | | DG SANTE & EFSA team | | |
| 08:30 – 09:30 (1h) | Institute of Microbiology and Parasitology, Faculty of Medicine, University of “Ss Cyril and Methodius”, Skopje <ul style="list-style-type: none"> - Introductory meeting at the director’s office of the IMP - Visit of the microbiology laboratory - Discussion with laboratory manager on AMR reporting, activities performed, type of antibiotic tested, Quality assurance. | <u>Location:</u> IMP Skopje | 08:30 – 11:00 (2h30) | Food Institute, Faculty of Veterinary medicine Skopje <ul style="list-style-type: none"> - Introductory meeting at the director’s office of the Food Institute (presentation of the OH country visit) - Visit of the microbiology lab (vet lab and food safety) <p>Presentation (EFSA): EU harmonised AMR monitoring in Zoonotic and Commensal bacteria in certain food producing-animals and food</p> <p>Discussions on AMR surveillance, prevention and control and research initiatives (veterinary and environmental sectors) and undergraduate education of veterinary medicine on AMR</p> | <u>Location:</u> FVM Skopje |
| 09:40 – 11:40 (2h) | University clinical centre “Mother Theresa” (University Hospital) <p>Introductory meeting with hospital managers and healthcare professionals from different wards/departments (surgery, adult ICU, paediatrics/neonatology, infectious diseases, infection control, and pharmacy)</p> <p>Visit to the respective departments of the hospital:</p> <ol style="list-style-type: none"> 1. University Clinic for Abdominal Surgery 2. University Clinic for Traumatology, Orthopaedics and Anaesthesia, Reanimation and Intensive Care with an Emergency Center (TOARILUC) 3. University Clinic for Paediatrics <p>Discussion during visit about prudent use/stewardships of antibiotics, AMR prevention and control measures, healthcare-associated infection / IPC guidelines, and related needs with hospital managers and healthcare professionals from different wards/departments (surgery, ICU, paediatrics/neonatology, infectious diseases, infection control, microbiology laboratory and pharmacy)</p> | <u>Location:</u> University Clinical Centre Mother Theresa | 11:15 – 13:00 (1h45) | Food Institute, Faculty of Veterinary medicine Skopje <p>Presentation:</p> <ul style="list-style-type: none"> - Monitoring of AMR in Food and food-producing animals - Monitoring of AMR in wastewater from slaughterhouses - AMR in clinical isolates from animals <p>Q&A/Discussion</p> | <u>Location:</u> FVM Skopje |
| 11:50 - | Visit to a community pharmacy (Eurofarm) pharmacy nearby to the MoH and IPH) | <u>Location:</u> EUROFARM, Skopje | | | |

DAY 2: Tuesday 30 January 2024

| | | | | | |
|--------------------|--|---|--------------------|--|--|
| 12:30 | Discussion on prudent use/stewardship of antibiotics, AM sales mechanism | | | | |
| 12:30 – 13:30 | Lunch Break | | 13:00 – 14:00 | Lunch Break | |
| 13:30 – 14:30 (1h) | North Macedonia Agency for drugs and medical devices Discussions on policy and regulation on the prudent use of AMR antibiotic and AMC monitoring in the human health sector ⁵ , on waste and disposal in the human health sector and Marketing-related issues (indicators in section 10), and current alignment plans with EU acquis and next steps | <u>Location:</u> The Macedonian Agency for Medicines and Medical Devices | 14:00 – 16:00 (2h) | The Food and Veterinary Agency (FVA) of North Macedonia Presentation: - the ESVAC/antimicrobial sales and use project in general - the collection of data Sales/Use from the Czech perspective Discussion on available data for antimicrobial sales and use and possibilities to obtain data (use by species) | <u>Location:</u> FVA meeting room |
| 14:30 – 16:30 (2h) | Institute of Public Health in North Macedonia - Short meeting at the director's office of the IPH (presentation of the OH country visit) - Visit of the microbiology lab Discussion (45min) on opportunities and challenges of AMR surveillance, electronic surveillance, prevention and control in human health, and challenges in implementing the One Health approach on AMR | <u>Location:</u> IPH | 16:00 – 18:00 (2h) | The Food and Veterinary Agency (FVA) of North Macedonia (continued visit) Presentations - Measures taken to encourage prudent use of antimicrobials in the veterinary sector - Biosecurity and Health plan (vaccination plan, endemic disease action plan, interventions) - Lessons learned from the Czech perspective Discussions on any measures taken to raise awareness of AMR among prescribers and animal keepers to encourage more prudent use of antimicrobials in production and companion animals. Discussion on the current EU VMP legislation and its AMR aspects (in terms of EU acquis). | <u>Location:</u> FVA meeting room |
| 17:00 – 18:00 (1h) | Meeting with GPs at a primary Health care center, Poliklinika Idadija, Skopje Discussion with General practitioners and Paediatricians about prudent use/stewardships of antibiotics, AMR prevention and control measures and related needs. | <u>Location:</u> Poliklinika IDADIJA | | | |

⁵ This agency does not covered antibiotic for use in the veterinary sector nor medicated feed

| DAY 3: Wednesday 31 January 2024 | | | | | |
|----------------------------------|---|--|-----------------------|--|---|
| ECDC team | | | DG SANTE & EFSA team) | | |
| Morning | <p>Visit to the Hospital for geriatrics and palliative medicine 13 Noemvri, Skopje</p> <p>Introductory meeting with healthcare professionals from different departments Visit to the respective departments of the hospital</p> <p>Discussion during visit about prudent use/stewardships of antibiotics, AMR prevention and control measures, healthcare associated infection / IPC guidelines, and related needs with hospital managers and healthcare professionals from different wards/departments)</p> | <p><u>Location:</u> Hospital for geriatrics and palliative medicine 13 Noemvri, Skopje</p> | Morning | <p>Meeting at the regional centre of FVA and Veterinary Practices, Kumanovo</p> <p>Discussion in the office of the regional veterinary services with veterinary inspectors on the official control on use of antimicrobial VMPs in animals and any measures taken locally to raise awareness of AMR and encourage the reduced and/or more prudent use of antimicrobials in production and companion animals</p> | <p><u>Location:</u> Regional center of FVA and Veterinary practices, Kumanovo</p> |
| | <p>Visit to regional clinical Hospital (Kumanovo City)</p> <p>Introductory meeting with hospital managers and healthcare professionals from different wards/departments (surgery, adult ICU, paediatrics/neonatology, infectious diseases, infection control, and pharmacy)</p> <p>Visit to the respective departments of the hospital.</p> <p>Discussion during visit about prudent use/stewardships of antibiotics, AMR prevention and control measures, healthcare-associated infection / IPC guidelines, and related needs with hospital managers and healthcare professionals from different wards/departments (surgery, ICU, paediatrics/neonatology, infectious diseases, infection control, microbiology laboratory and pharmacy)</p> | <p><u>Location:</u> Kumanovo Regional Hospital</p> | | <p>Meeting at the regional centre of FVA and Veterinary Practices</p> <p>Presentation: The Czech experience promoting prudent use of antimicrobials in animals</p> <p>Discussion in the office of the regional veterinary services with local farmers, practicing veterinarians and veterinary inspectors on actions taken locally and/or by the stakeholders to reduce the use of antimicrobials / use antimicrobials more prudently in food-production and companion animals.</p> | |
| 13:00 – 14:00 | Lunch Break | | | | |
| 14:00 – 15:00 (1h) | <p>Visit of the public health laboratory nearby Kumanovo Regional Clinical Hospital</p> <p>Discussion with laboratory manager on AMR reporting, activities performed, type of antibiotic tested, Quality assurance.</p> | <p><u>Location:</u> Kumanovo Regional PH Laboratory</p> | | | |
| 15:00 – 16:00 (1h) | <p>Visit to a community pharmacy</p> <p>Discussion on prudent use/stewardship of antibiotics, AM sales mechanism</p> <p>Moderator: Aikaterini Mougkou</p> | <p><u>Location:</u> Close to the hospital</p> | | | |

DAY 4: Thursday 1 February 2024

| ECDC team | | DG SANTE & EFSA team | |
|----------------------|---|---|--|
| 08:30 – 11:00 (2.5h) | <p>Visit of Adzibadem Sistina private hospital, Skopje</p> <p>Introductory meeting with hospital managers and healthcare professionals from different wards/departments (surgery, adult ICU, infectious diseases, infection control, microbiology laboratory and pharmacy)</p> <p>Visit to the respective departments of the hospital</p> <p>Discussion during visit about prudent use/stewardships of antibiotics, AMR prevention and control measures, healthcare associated infection / IPC guidelines, and related needs with hospital managers and healthcare professionals from different wards/departments (surgery, ICU, infectious diseases, paediatrics/neonatology, infection control, microbiology laboratory and pharmacy)</p> | <p><u>Location:</u> Adzibadem Sistina Hospital</p> | <p>08:30 – 10:30 (2h)</p> <p>Faculty of Veterinary medicine Skopje</p> <p>Presentation Education on AMR in curriculum of health professional and antibiotic awareness activities</p> <p>Discussion: undergraduate education on AMR under One Health perspective</p> <p><u>Location:</u> FVM</p> |
| 13:00 – 14:00 | | | |
| 14:00 – 17:00 | Visiting team will prepare for the closing meeting /preliminary report preparation | | |

DAY 5: Friday 2 February 2024

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|---------------|---|--|
| 08:30 – 12:00 | <p>Closing meeting with the national authorities:</p> <ul style="list-style-type: none"> - Ministry of Health/ Ministry of Agriculture, Natural Resources and Environment and relevant agencies and stakeholders - Technical experts from national institutions, including the members of MCCAMR | <p><u>Location:</u> IPH meeting room building</p> |
|---------------|---|--|

Annex 2. List of ECDC antibiotic awareness materials to be translated by ECDC into Macedonian and Albanian for potential use in North Macedonia

The following ECDC EAAD materials could be translated into Macedonian and Albanian languages for potential use during national campaigns in North Macedonia:

(<https://antibiotic.ecdc.europa.eu/en/plan-campaign>)

- [Communication toolkit to promote prudent antibiotic use aimed at **primary care prescribers**](#)
- [Communication toolkit for **professionals in hospitals and other healthcare settings**](#)
- [Communication toolkit to promote prudent antibiotic use with focus on **self-medication with antibiotics**](#)
- [Communication toolkit to promote prudent antibiotic use aimed at **general public**](#)
- [Toolkit for engaging in **social media activities** promoting prudent antibiotic use](#)

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