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FINAL JOINT REPORT IN RESPECT OF A ONE HEALTH COUNTRY VISIT TO BULGARIA FROM 15 OCTOBER 2018 TO 19 OCTOBER 2018 TO DISCUSS POLICIES RELATING TO ANTIMICROBIAL RESISTANCE

In response to information provided by the competent authority, any clarification appears in the form of a footnote.

Executive Summary

The European Centre for Disease Prevention and Control (ECDC) and the European Commission's Directorate General for Health and Food Safety jointly carried out this country visit to Bulgaria from 15 to 19 October 2018. The visit was carried out following the invitation from the competent authorities to assist them in the preparation of their national strategy for tackling antimicrobial resistance (AMR) based on a 'One Health' perspective.

Overall, the report concludes that there are numerous gaps and weaknesses in the approach towards tackling AMR in Bulgaria, both in the veterinary and human health domains, which compare poorly with the situation in other Member States. There is in particular a significant lack of communication and collaboration between the veterinary, human health and environmental authorities in a One Health perspective. There is no Inter-sectoral One Health Coordinating Mechanism on AMR, and draft national action plans for animal health and for human health, which are in various stages of development, have been developed separately.

In the human area, the current levels of AMR are of concern. There seems to be limited knowledge about AMR in healthcare professionals on all levels. This is underlined by a lack of understanding of the extent of the issue of AMR and of the urgency to effectively manage and control AMR in the country. There also appear to be constraints in hospitals in terms of infrastructure, resources and a shortage in key healthcare personnel in various domains. If appropriate measures are not taken and the current trends of AMR continue, it is likely that untreatable healthcare-associated infections will become a reality, with an impact on the ability of hospitals to provide important medical services such as major surgical procedures, cancer treatment and intensive care.

In the veterinary area, awareness concerning AMR matters is generally very low and few effective initiatives have been taken by the national authorities to date, which stated that this was due to the existence of other pressing work priorities, such as dealing with cases of African Swine Fever.

The report outlines various considerations which could be helpful in reviewing and implementing a national AMR strategy.

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ABBREVIATIONS AND DEFINITIONS USED IN THIS REPORT

Abbreviation	Explanation
AMR	Antimicrobial resistance
AST	Antimicrobial susceptibility testing
BAM	Bulgarian Association of Microbiologists
BFSA	Bulgarian Food Safety Agency
BMA	Bulgarian Medicines Agency
BulSTAR	Bulgarian Surveillance Tracking of Antimicrobial Resistance
BulNoso	Bulgarian Association for Infection Prevention and Control
BVU	Bulgarian Veterinary Union
CIA	Critically important antimicrobial
CPE	Carbapenemase producing Enterobacteriaceae
EAAD	European Antibiotic Awareness Day
EARS-Net	European Antimicrobial Resistance Surveillance Network
ECDC	European Centre for Disease Prevention and Control
EFPIA	European Federation of Pharmaceutical Industries and Associations
EFSA	European Food Safety Authority
EMA	European Medicines Agency
EQA	External quality assessment
ESAC-Net	European Surveillance of Antimicrobial Consumption Network
ESBL	Extended-spectrum beta-lactamase
ESVAC	European Surveillance of Veterinary Antimicrobial Consumption
EU	European Union
EUCAST	European Committee on Antimicrobial Susceptibility Testing
FAO	Food and Agriculture Organization
GP	General practitioner
HAI	Healthcare-associated infection
HAI-Net	Healthcare-Associated Infections surveillance Network
ICM	Inter-sectoral coordinating mechanism
IPC	Infection prevention and control
JAMRAI	Joint Action on AMR and healthcare-associated infections
MDRO	Multidrug-resistant organism
MRSA	Methicillin-resistant *Staphylococcus aureus*

Abbreviation	Explanation
NCIPD	National Centre of Infectious and Parasitic Diseases
NCPHA	National Centre for Public Health and Analyses
NRC-HAI	National Reference Centre on healthcare-associated infections
NRL	National Reference Laboratory
NRLARCM	National Reference Centre on AMR and Antimicrobial Use
OIE	World Organisation for Animal Health
PCU	Population correction unit
SPC	Summary of product characteristics
VMP	Veterinary medicinal product
VRE	Vancomycin-resistant Enterococci
WGS	Whole genome sequencing
WHO	World Health Organization

1 INTRODUCTION

The European Centre for Disease Prevention and Control (ECDC) and the European Commission's Directorate-General for Health and Food Safety were invited by the Bulgarian authorities to carry out jointly a country visit from 15 to 19 October 2018. The overall aim of the visit was to follow-up on the Commission's One Health Action Plan against antimicrobial resistance (AMR) published on 29 June 2017 [1], in particular by assisting Bulgaria in further developing and implementing its national strategies and policies against AMR based on a One Health perspective.

The ECDC team focussed on the human health aspects of AMR while the Commission team concerned itself with veterinary aspects and, to a limited extent, environmental aspects. Both teams included national experts from other European Union (EU) Member States. This report brings together the main observations and conclusions of the two teams and identifies areas where further developments could be beneficial.

An opening meeting was held on 15 October. At this meeting the objectives and scope of, and itinerary for, the country visit were confirmed.

2 OBJECTIVES AND SCOPE

The overall objective of this country visit was to assist Bulgaria in further developing and implementing its national strategies and policies against AMR based on a One Health perspective. This objective involved (a) discussing with the relevant competent authorities and national professional and industry stakeholders the situation regarding the prevention and control of AMR, and (b) exchanging information on examples of good practice implemented by Bulgaria and other Member States in addressing these issues which could potentially be helpful in further developing and implementing national AMR strategies.

The scope of the joint country visit was as follows:

- For the human aspects of AMR, the visit focussed on the control of AMR through the prudent use of antimicrobials, and infection prevention and control (IPC).
- For the veterinary aspects of AMR, the visit focussed on the policies to tackle AMR through the reduced and more prudent use of antimicrobials, as advocated in the relevant EU guidelines for prudent use of antimicrobials in veterinary medicine [2].
- The discussions on the national AMR strategies, action plans and inter-sectoral coordination and cooperation took into account relevant guidance and documentation, including that jointly adopted by the World Health Organization (WHO), the Food and Agriculture Organization (FAO) of the United Nations, the World Organisation for Animal Health (OIE) [3], the European Medicines Agency (EMA) [4] and the European Food Safety Authority (EFSA) [5].

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1 https://ec.europa.eu/health/amr/sites/amr/files/amr_action_plan_2017_en.pdf
2 http://ec.europa.eu/health/antimicrobial_resistance/docs/2015_prudent_use_guidelines_en.pdf.
3 http://apps.who.int/iris/handle/10665/204470
4 http://www.ema.europa.eu/ema/index.jsp?curl=pages/special_topics/general/general_content_000439.jsp&

The implementation of the requirements of Commission Implementing Decision 2013/652/EU on the monitoring and reporting of AMR in zoonotic and commensal bacteria was not included in the scope of this visit [6].

In pursuit of these objectives, the following meetings and visits took place:

Visits / Meetings		No.	Comments
Competent authority	Central	2	Joint opening and closing meetings with the Ministry of Health, the Ministry of Agriculture, Food and Forestry, the Ministry of Environment and Water, the Bulgarian Food Safety Agency (BFSA) and the National Centre of Infectious and Parasitic Diseases (NCIPD)
Veterinary and environmental aspects			
Competent authority		1	Ministry of Agriculture, Food and Forestry Ministry of Environment and Water BFSA
Industry stakeholders		1	Meetings with Bulgarian Veterinary Union (BVU), Bulgarian Union of Poultry Breeders, Association of producers and wholesalers of veterinary medicinal products (VMPs), producers of compound animal feed (including medicated feed), small animal veterinary practitioners and integrated poultry breeding company
Veterinary practices		1	One clinic treating pet animals
Farms		2	One pig and one dairy farm
Laboratory		1	National Diagnostic and Research Veterinary Medical Institute, the National Reference Laboratory (NRL) on AMR
Human health aspects			
Competent authority		5	Separate meetings with the Ministry of Health, the NCIPD, the National Health Insurance Fund, the Bulgarian Medicines Agency (BMA), and one Regional Health Authority
Hospitals		2	Military Medical Academy Sofia (including microbiology laboratory, intensive care unit and infectious diseases ward), and University hospital St. Georgi, Plovidv (including the microbiology laboratory, intensive care unit and hospital pharmacy)
General practitioners (GPs)		1	One GP group practice in Plovdiv
Community pharmacists			Two community pharmacies (Sofia, Plovdiv)
Professional associations		2	Separate meetings with the Bulgarian Association for Infection Prevention and Control (BulNoso) and the Bulgarian Pharmaceutical Union

Concerning the human health elements of the joint visit, the Council Recommendation of 15 November 2001 on the prudent use of antimicrobial agents in human medicine (2002/77/EC) outlines the threat that AMR poses to human health and advocates for a range of actions to be taken for its prevention and control. Council Conclusions on AMR of 10 June 2008 reiterated this call for action.

To assist Member States in implementing the Council Recommendation, ECDC has developed a process for and is carrying out, upon invitation from national authorities, country visits to specifically discuss and assess the situation of the country regarding prevention and control of AMR through the prudent use of antibiotics and infection control. These country visits also help document how Member States have approached this implementation and

mid=WC0b01ac0580a7815

5 https://www.efsa.europa.eu/en/topics/topic/antimicrobial-resistance

6 This was the subject of an audit by the Directorate-General for Health and Food Safety in 2017 (reference DG(SANTE) 2017-6194: http://ec.europa.eu/food/audits-analysis/audit_reports/details.cfm?rep_id=3809

deployed national activities and support the European Commission in evaluating this implementation.

To help the ECDC team ensure consistency of the visits and follow-up of progress of countries, an assessment tool has been developed. The assessment tool includes 10 topics. These topics are regarded as core areas for successful prevention and control of AMR and are based on Council Recommendation 2002/77/EC and on Council Conclusions of 10 June 2008. The assessment tool is used as a guide for discussions during the visit.

3 BACKGROUND

Joint country visits are one of the many initiatives set out in the Commission's One Health Action Plan against AMR [1] and contribute to its aim of making the EU a best practice region in the fight against AMR. The term 'One Health' recognises that human and animal health are interconnected, that diseases are transmitted from one to the other and the threat of AMR should be tackled in both. The One Health approach also encompasses the environment, another link between humans and animals and likewise a potential source of new resistant organisms. The importance of adopting a One Health approach to tackling AMR has been recognised globally, notably by the WHO Assembly which urged all its country members, including EU Member States, to develop and have in place by 2017 national action plans on AMR that are aligned with the objectives of the WHO global action plan on AMR, adopted at the 68th World Health Assembly in May 2015 [7].

Joint country visits aim at supporting Member States in the design and implementation of their national AMR action plans, and the visits build upon previous work carried out by the ECDC and the Commission:

- In the area of human health, ECDC developed a process of country visits to discuss and assess the situation regarding the prevention and control of AMR through the prudent use of antibiotics and infection control. These are based on Council Recommendation 2002/77/EC on the prudent use of antimicrobial agents in human medicine, which advocates a range of actions to be taken to prevent and control the development of AMR. The Council conclusions on AMR of 10 June 2008 [8] reiterated the call for action to tackle AMR. In June 2009, EU health ministers adopted a Council Recommendation on patient safety including the prevention and control of healthcare-associated infections [9], which further stressed the importance of combating AMR as a patient safety issue. In response to a call contained in the Council Conclusions on the next steps under a One Health approach to tackle AMR of July 2016 [10], EU guidelines on the prudent use of antimicrobials in human medicine were published in June 2017 [11].

7 http://www.who.int/antimicrobial-resistance/national-action-plans/en/
8 http://www.consilium.europa.eu/ueDocs/cms_Data/docs/pressData/en/lsa/101035.pdf
9 https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=OJ%3AC%3A2009%3A151%3ATOC
10 https://publications.europa.eu/en/publication-detail/-/publication/963104ce-5096-11e6-89bd-01aa75ed71a1/language-en
11 https://eur-lex.europa.eu/legal-content/EN/ALL/?uri=OJ%3AC%3A2017%3A212%3ATOC

– In the veterinary area and as part of the Commission's work to tackle AMR, the Directorate for Health and food audits and analysis of the Directorate-General for Health and Food Safety has been carrying out a project on the Member States' measures to tackle AMR relating to the use of veterinary medicines, including the identification of examples of good practice which could potentially be helpful to other Member States in addressing this issue. This work took into account the above-mentioned guidelines for prudent use of antimicrobials in veterinary medicine, which were published in 2015. An overview report on this project has been already published in 2018 [12], with a final overview report expected in 2019. In addition, the afore-mentioned Directorate has been carrying out a series of audits on the implementation of the requirements laid down in Decision 2013/652/EU, and an interim overview report on this series has been already published in 2017 [13] with a final overview report expected in 2019.

ECDC's mission, as part of its Founding Regulation No 851/2004, is (i) to identify, assess and communicate current and emerging threats to human health from communicable diseases; (ii) in the case of other outbreaks of illness of unknown origin which may spread within or to the Community, the Centre shall act on its own initiative until the source of the outbreak is known; and (iii) in the case of an outbreak which clearly is not caused by a communicable disease, the Centre shall act only in cooperation with the competent authority upon request from that authority. As part of this mission, ECDC may be requested, by the European Commission, a Member State, or another country to provide scientific or technical assistance in any field within its mission.

ECDC and EFSA have published a summary report on AMR in bacteria from humans, animals and food, including data from Bulgaria (European Union summary report on AMR in zoonotic and indicator bacteria from humans, animals and food in 2016 [14]). ECDC, EFSA and EMA have also issued a joint report on the integrated analysis of the consumption of antimicrobial agents and occurrence of AMR in bacteria from humans and food producing animals (Joint Interagency Antimicrobial Consumption and Resistance Analysis report – JIACRA II), including data from Bulgaria [15]. These reports largely draw conclusions for the EU as a whole based on the complete range of data available.

4 OBSERVATIONS AND CONCLUSIONS

4.1 AMR STRATEGIES, ACTION PLANS AND COORDINATION, IN A ONE HEALTH CONTEXT

4.1.1 National strategies and action plans on AMR

1. At the time of the visit, Bulgaria did not yet have a finalised national AMR strategy or action plan in place. During the opening meeting, the visit teams were informed that a "National programme for rational use of antibiotics and antibiotic resistance surveillance

12 https://publications.europa.eu/en/publication-detail/-/publication/aa676ddd-2d87-11e8-b5fe-01aa75ed71a1/language-en
13 http://ec.europa.eu/food/audits-analysis/audit_reports/index.cfm
14 https://www.efsa.europa.eu/en/efsajournal/pub/5182
15 http://www.ema.europa.eu/docs/en_GB/document_library/Report/2017/07/WC500232336.pdf

(2017 – 2021)", covering the human health area, was submitted by the NCIPD to the Ministry of Health in December 2016. This draft programme was developed following discussions involving representatives of the Ministry of Health, BFSA, WHO/Europe, universities and patient safety non-governmental organisations [16].

2. At the time of the joint visit, this draft national programme had not yet been finalised. The draft programme emphasises the need to contain AMR by implementation of a One Health approach, which includes concerted actions in human medicine as well as in veterinary medicine and in the food industry. The draft programme also highlights the need for formation of a national inter-sectoral expert committee on rational antibiotic policy including representatives from the Ministry of Health, the National Health Insurance fund, the BMA, the pharmaceutical industry, veterinary medicine and agriculture, non-governmental and patient organisations and medical experts in the field of antibiotic use and surveillance of infections and AMR. The draft programme further includes a detailed list of relevant key stakeholders and proposes several actions on the overarching topics of standardisation and monitoring of the work in the clinical microbiology laboratory, AMR surveillance, rational antibiotic policy and other aspects. However, this draft programme has not been formally adopted and actions on pursuing the objectives were therefore not started.

3. Concerning veterinary aspects, a BFSA Order of 2017 confirmed the establishment of an Expert Committee on AMR. No human health experts were included in this Committee. On 1 October 2018, a draft national action plan on AMR for the veterinary and food sectors was published on the BFSA website [17] for consultation for a period of 1 month, with no comments having been received by the time of the visit. This draft national action plan also envisages the establishment of a One Health coordination group consisting of the Ministry of Agriculture, the Ministry of Health and the Ministry of the Environment. At the visit's opening meeting, the human health authorities stated that they were unaware of this draft action plan for the veterinary and food sectors and had not been involved in its preparation, even though some of the proposed actions related to general topics such as communication and awareness-raising, which would encompass both the human health and veterinary areas.

4. The draft veterinary-food AMR action plan is based on the WHO guidance in setting out strategic goals, associated strategic actions and specific activities and some indication of responsibilities and budgetary requirements to implement the plan. According to BFSA, there are adequate personnel resources available to carry out its tasks in relation to this draft AMR action plan.

5. The scope of the draft action plan is largely limited to food-producing animals and, even if it remains as a sectoral veterinary-food plan, it would benefit from incorporating other relevant issues – notably AMR for companion animals (pets and horses). This is

[16] https://ncipd.org/index.php?option=com_k2&view=item&id=311:kragla-masa-natzionalna-programa-za-ratzionalna-upotreba-na-abtibiotitzite-i-nadzor-na-antimikrobnata-rezistentnost-amr-v-balgariya-proekt&lang=bg

[17] http://www.babh.government.bg/bgPage/antimicrobial_resistance/index/antimicrobial_resistance/Антимикроб

particularly relevant, given that small animal veterinary practitioners met by the Commission team reported regular treatment failures involving antimicrobials, resulting in the need to significantly increase the dose of antimicrobial above that shown in the summary of product characteristics (SPC), as well as the results of AMR tests indicating the presence of multi-drug resistance in pets, with the associated potential implications for human health.

6. Environmental issues receive little attention in the draft veterinary-food action plan, which is often the case in other Member States also. It would be useful for the Bulgarian authorities and relevant stakeholders to follow the output of initiatives such as the Joint Programming Initiative on AMR [18], which is helping to identify knowledge gaps and priorities for future research and development and specific work activities in this area.

4.1.2 Multi-sectoral collaboration and coordination, including One Health approach

7. AMR is considered as a high priority by decision makers at the Ministry of Health and Ministry of Agriculture. Nevertheless, an Inter-sectoral Coordinating Mechanism[19] to develop a national action plan and antibiotic policies, raise awareness with regard to AMR issues, and formulate recommendations and guidelines for diagnosis, consumption and prescription of antibiotics, was not in place in Bulgaria at the time of this visit. There is little evidence of coordinated, effective or One Health initiatives to address AMR. One Bulgarian institute, the National Centre of Infectious and Parasitic Diseases (NCIPD), is currently signed up to participate in the EU Joint Action on AMR and healthcare-associated infections (JAMRAI) [20]. The visit teams were informed that this institute is considering withdrawing from the Joint Action owing to their limited availability of funds.

8. There has been very little, if any, involvement of the industry or the organisations representing the veterinary profession in the preparation of the draft veterinary-food AMR action plan. The Commission team was informed that stakeholders representing meat processors, milk producers and cattle farmers were not interested or available to attend the Commission team's meeting with stakeholders in order to discuss any aspects related to AMR or the prudent use of antimicrobials. In some other Member States, stakeholders representing such key sectors have shown a greater interest to be involved in AMR issues, and they normally play an important role in tackling AMR.

9. The Commission team met with the associations of producers and wholesalers of VMPs, manufacturers of compound animal feed (including medicated feed), the BVU, small animal veterinary practitioners, the Hungarian Poultry Union and representatives of a large integrated poultry company. Some of these stakeholders expressed frustration at a lack of awareness and effective actions in Bulgaria concerning AMR.

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18 https://www.jpiamr.eu/
19 As recommended by Council Recommendation 2002/77/EC.
20 https://eu-jamrai.eu/

10. Taking a broader One Health perspective, there is a proposal within the draft veterinary-food AMR action plan to develop a coordination body with the human health colleagues which would help to identify synergies and common issues. However, the Commission team noted that this should ideally have been put in place at an earlier stage when the shape of the sector plans could have been more easily influenced.

11. The competent authorities pointed out that, even if a multi-disciplinary AMR action plan is developed with the involvement of participants from a number of Ministries, the specific responsibilities are attributed to each responsible Ministry (alongside the financial resources for the individual actions), meaning that it would be difficult for one Ministry to allocate funds to a cross-cutting action which would involve also other Ministries. The Commission team noted that this constraint may pose an obstacle to a truly One Health and holistic approach to tackling AMR.

12. For the veterinary and environmental aspects of AMR the Commission team was not informed of any specific multi-disciplinary or multi-sectoral collaboration existing at local level to promote effective actions to address AMR in a One Health perspective. In other Member States, such initiatives have been taken at a local level to coordinate the implementation of a national AMR strategy, involving participants from the human health, veterinary and environmental sectors.

13. Concerning human health aspects of AMR, an antimicrobial stewardship team including experts from different specialties (microbiologist, pharmacist, clinicians) was in place in one visited hospital. This team had analysed the local antimicrobial consumption and AMR data and identified high consumption of third-generation cephalosporins and meropenem as an important problem. In response, this team had developed a local guideline for the most common infections available as a pocket book and implemented restrictions on antimicrobial prescription on different levels, with the most restricted antibiotics (including third-generation cephalosporins and meropenem) only being made available after authorisation by a member of the antimicrobial stewardship team after consulting a clinical microbiologist. In another visited hospital, antimicrobial treatment guidelines had also been developed for different syndromes by a committee that included clinicians. The ECDC team cannot generalise whether such practices are in place in all or in the majority of health care facilities in the country.

14. In the visited region, there was no community-based activity to reduce antimicrobial consumption or improve information sharing with medical professionals. In a large outpatient clinic, including the practices of more than 80 general practitioners (GPs) and specialists and a related microbiology laboratory, there was no activity to analyse the antimicrobial susceptibility data available from the laboratory and to provide it to GPs to improve their choice of antimicrobial therapy. For their choice of antimicrobial therapy, the physicians mainly relied on clinical experience. Difficult-to-treat infections were not regularly discussed among physicians belonging to the same practice and there was no exchange of ideas on treatment approaches and prudent use of antibiotics. Monitoring and control of AMR was also not in place for the long-term care facilities. Each resident at such a facility has the choice of being cared for by their own GP, which may result in

an inconsistent approach to the diagnosis and management of infections within the facility.

15. The visited local health authority did not hold any data on antimicrobial consumption or AMR (except for notified cases of Healthcare-Associated Infections (HAIs) that could provide a basis for regional activities to better target antimicrobial use. Collaboration between regional health authorities and with community pharmacies was not mentioned during the visit. Cooperation with animal health authorities would be activated in case of outbreak, but regular exchange of data on AMR and antimicrobial consumption was not described. Multidisciplinary committees or working groups related to AMR were not in place within the visited county public health authority.

4.2 HUMAN ASPECTS OF AMR

4.2.1 Laboratory capacity

16. The NCIPD is responsible for surveillance, risk assessment and guidance regarding communicable diseases. It has four departments and 17 reference laboratories, eight of these related to microbiology. In addition, there are seven reference centres, including the "National Reference Centre on AMR and Antimicrobial Use" (NRLARCM). This reference centre is responsible for all reference activities related to AMR, including diagnostics, staff training, evaluation and certification of microbiological laboratories, national surveillance of AMR, and reporting of antimicrobial consumption data to the European Surveillance of Antimicrobial Consumption Network (ESAC-Net). Reporting of AMR to the European Antimicrobial Resistance Surveillance Network (EARS-Net) is performed directly by certified clinical microbiology laboratories, on a voluntary basis. The NRLARCM is supported through 28 regional laboratories which are under the authority of the Regional Health Inspectorates. Most of these regional laboratories are accredited.

17. Hospitals are served by local microbiology laboratories that are certified through the NCIPD. The NCIPD external quality assessment (EQA) exercise is organised in three levels of difficulty according to the type of laboratory (university laboratory, hospital laboratory, or private laboratory) and consists of the identification and antimicrobial susceptibility testing (AST) of five strains. The EQA exercise is repeated twice yearly (spring and autumn). Some laboratories also participate in the UK-NEQAS EQA exercises.

18. All local laboratories perform phenotypic susceptibility testing and larger laboratories often use semi-automated systems for this purpose. Since 2015, all Bulgarian laboratories follow the definitions of the European Committee on Antimicrobial Susceptibility Testing (EUCAST). A few local laboratories also perform molecular characterisation of isolates, mainly in the case of outbreaks. The NRLARCM performs molecular typing and characterisation of strains sent from the microbial laboratories using PCR-based methods or whole genome sequencing (WGS). The turn-over time for provision of results from the NRLARCM to the sender is 4-7 days. Since 2002,

reference testing has included extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae and CPE, carbapenem-resistant *Acinetobacter baumannii*, MRSA, VRE, and since 2018 also colistin resistance in CPE. Testing for colistin resistance in local laboratories is performed mainly using semi-automated systems, but microbroth dilution is available at the NRLARCM. The *mcr* genes have so far not been detected. Sending isolates for testing to NRLARCM does not result in any additional cost for the local laboratories sending isolates; however, many microbiology laboratories still do not use this service, even in outbreak situations.

4.2.2 Monitoring of AMR in human health

19. Since 1997, Bulgaria has established a national surveillance system of AMR (BulSTAR - Bulgarian Surveillance Tracking of Antimicrobial Resistance) in collaboration with the Bulgarian Association of Microbiologists (BAM). This activity is run in the Department of Microbiology at the NCIPD. Data from the reports of all participants in BulSTAR are analysed at the NRLARCM. BulSTAR has increased its coverage over time and included, in 2017, 143 of 305 laboratories operating in the country. BulSTAR collects AMR data on a wide range of specimens including blood cultures in an aggregated format. For this reason, it is not possible to convert those data to the EARS-Net isolate-based format. BulSTAR provides annual reports with AMR results aggregated at national level; these reports are hosted on the BAM website.

20. Bulgaria participates in European surveillance of AMR (EARS-Net) with a subsample of about 20 BulSTAR laboratories that follow the EARS-Net protocol, participate in the EARS-Net EQA scheme and report data to EARS-Net on a voluntary basis. These laboratories mainly serve university and tertiary hospitals. For this reason, results from small hospitals, where AMR proportions are possibly lower, are underrepresented. This, together with the low blood culture rate observed in hospitals that contribute data to EARS-Net and in the ECDC point prevalence survey in acute care hospitals, makes it likely that the overall AMR situation of the country is different from the one currently reported by EARS-Net.

21. In the two visited tertiary hospitals, the hospital AMR data were used to produce internal reports and to provide feed-back to the departments on the local epidemiology. However, AMR data were not systematically communicated to the IPC team for timely action to provide support in controlling outbreaks and preventing further spread of multidrug-resistant organisms (MDROs).

4.2.1 Monitoring of antibiotic usage in human health

22. Antimicrobial consumption data of Bulgaria are regularly reported to ESAC-Net. This reporting is based on data on medicines bought by community and hospitals pharmacies from wholesalers provided to the NCIPD by IQVIATM (formerly IMS Health and Quintiles). In the community, data are not available at patient level as prescriptions issued to non-hospitalised patients are, for the main part, not reimbursed. The data source does not allow to evaluate completeness of data and antimicrobial consumption

in the country may be underestimated. Data per diagnosis are not available and feed-back on prescription patterns cannot be provided to prescribers [21].

23. In hospitals, hospital pharmacies can, from their information systems, provide detailed information at patient level on antibiotic prescriptions delivered to hospitalised patients for treatment or prophylaxis. These data are currently not transferred to the national level, but can be used in the hospitals to provide clinical departments with specific results on antibiotic use. In the two hospitals that were visited, detailed antimicrobial consumption data were available and used to produce internal reports. These reports could be used to inform antimicrobial stewardship activities in the hospitals.

4.2.2 Antibiotic utilisation and treatment guidance in human health

24. For hospitals, antimicrobial treatment is not reimbursed directly but as part of clinical pathways which determine the reimbursement of hospital care. If a patient needs more extensive treatment than calculated in the corresponding clinical pathway, the hospital must bear the additional cost. Antimicrobial stewardship is mandatory for hospitals and is managed by a local team, consisting of microbiology and epidemiology experts supported by the hospital management. Provision of advice related to antimicrobial stewardship is mainly a task of medical doctors; however, infectious disease physicians or microbiologists are not always available in hospitals.

25. In the community, antibiotic treatment is mainly paid directly by patients with only a few exceptions to this rule, for example for children. Patient payment, however, does not limit access to or prevent excessive use of antibiotics because antibiotics, including oral broad-spectrum antibiotics, are available at very low cost. Dispensing antibiotics without a medical prescription is illegal; however, there was disagreement among professionals as to which extent it is still possible to obtain antibiotics without prescription in Bulgarian pharmacies. At the time of the visit, the inspectors of the BMA had detected about 50 related violations in pharmacies in 2018; however, only a small proportion of the 4 000 Bulgarian pharmacies can be visited by inspectors each year. In addition, the BMA does not have the resources to perform follow-up visits of pharmacies to evaluate if compliance improved after an initial visit [22].

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21 In their response to the draft report the competent authority noted that the pharmacist undertakes to record each prescription delivered in a logbook which may be in either paper or electronic form and that it is not mandatory to record the treatment prescribed. Available software in community pharmacies can be consulted on the consumption of a specific product by brand name.

22 In their response to the draft report the competent authority noted that under the legislation currently in force in Bulgaria, only practising doctors/dental practitioners have the right to prescribe medicinal products, including antimicrobials. Only pharmacists have the right to deliver prescription medicines. The Ministry of Health, the Bulgarian Drug Agency, the regional health inspectorates and the National Health Insurance Fund (for fully or partially reimbursed medicinal products) control the implementation of legislative provisions on the prescription and dispensing of medicinal products for human use in Bulgaria. In addition, pharmacists are held liable for breaches committed in the exercise of their profession in the event of failure to comply with the rules laid down in the Code of conduct of pharmacists and the rules of good pharmaceutical practice controlled by the Medical Supervision Executive Agency and the Bulgarian Pharmaceutical Union (the respective ethics committee of the regional order of pharmacists following a report by its members).

26. There are no national guidelines for the treatment of common infections in the community or the hospital sector, with the exception of a guideline on surgical prophylaxis that was developed in 2009. No other antimicrobial treatment guideline seems to be offered by medical unions or professional medical or microbiology societies. Guidelines from international societies, guidelines of other countries or treatment guides such as the Sanford guide were not mentioned by physicians as resources for information on antimicrobial treatment. Instead, the physicians that we met stated that they mainly rely on their clinical experience or even on information from pharmaceutical industry representatives to determine their choice of antimicrobial treatment. The physicians met had not recently attended any seminar or other continuing education on AMR-related topics and national conferences. Meetings of physician's associations were the only mentioned opportunities for exchange of information on antibiotics and AMR.

4.2.3 Infection prevention and control in human health

27. Within the legal framework all hospitals are required to have an IPC team that should ideally be composed of a nurse, a microbiologist/infectious disease specialist and an epidemiologist. This IPC team is responsible for the daily management of hospital hygiene. In addition, there is an IPC committee in every hospital with the role to liaise with the Regional Health Inspectorate to report cases of HAIs or outbreaks. The National Insurance Fund will not sign any contract with hospitals that do not have the appropriate IPC requirements in place.

28. In the visited hospital wards, there was a shortage of single rooms for patient isolation. The placement of alcohol-based handrub dispensers was not optimal in most areas and did not follow the principle of having alcohol-based handrub available at the point of care.

29. At regional level, there are 28 Regional Health Inspectorates that are among other tasks, in charge of the reporting of HAIs. The Regional Health Inspectorates receive information on HAIs from the hospitals in the regions according to a list of reportable infections. However, MDROs are not included in this list. Data collected by the Regional Health Inspectorates are transferred to the National Centre for Public Health and Analyses (NCPHA). This centre then provides aggregated data to the national reference centre on HAI (NRC-HAI) at NCIPD for further analysis. The Regional Health Inspectorate can also perform audits in the hospitals. In the visited region, one-week audits were performed for each of the 36 hospitals once per year and followed a pre-specified catalogue of elements to be evaluated.

30. The NRC-HAI has the mandate to perform surveillance and to analyse the incoming HAI data. Apart from the ECDC point prevalence survey of HAIs and antimicrobial use in acute care hospitals, Bulgaria does not participate in other HAI surveillance modules as part of the Healthcare-Associated Infections surveillance Network (HAI-Net). Surveillance of HAIs is mandatory for Bulgarian hospitals; however, there is no functional system in place to detect and report outbreaks of HAIs in due time. For

example, a large multidrug-resistant *A. baumannii* outbreak in one hospital was not known to the Regional Health Authorities. The NCR-HAI also includes a laboratory for disinfection, sterilisation and bio-indicators.

31. The Bulgarian Association for Infection Prevention and Control (BulNoso) was established in 2003 as a result of collaboration between the Bulgarian Ministry of Health and Switzerland. As of 2017, BulNoso had 723 individual and 39 corporate members (hospitals). BulNoso publishes an official journal available on its website (www.bulnoso.org) and organises annual national symposia (seven symposia so far), regional educational seminars on IPC and occupational health as well as round table discussions with national clinical associations. National consensus guidelines based on European standards and signed by BulNoso and other medical societies have been developed, for example for the prevention of surgical site infections, urinary tract infections and catheter-associated bloodstream infections. BulNoso also participates in the WHO patient safety challenge "Clean care is safer care". Two hand hygiene campaigns have already been performed and a third campaign is planned for 2018-2020.

32. There is a national standard on HAI prevention and control published in the national state gazette. A national action plan on IPC, prepared by BulNoso is about to be completed. In addition, IPC/hygiene is also mentioned in the draft "National programme for rational use of antibiotics and antibiotic resistance surveillance (2017 – 2021)" developed by the NCIPD.

4.2.4 Educational programmes on AMR

33. In Bulgaria, medical studies include AMR lectures in the microbiology course in the 2nd and 3rd year of studies. Pharmacy studies follow a state curriculum and the pharmacotherapy course includes lectures on AMR and antibiotic policy. A microbiology course is also part of the pharmacy training. For medical doctors, IPC training is provided in the epidemiology and microbiology courses. For nurses, there are 30 hours of IPC as part of basic education. A diploma in IPC is also offered for nurses. Organisation of the IPC course and related diploma is provided by the government, while the curriculum is developed and faculty is provided by BulNoso. This diploma consists of a two-year programme centralised in Sofia and mainly based on workshops. So far, 165 IPC nurses have graduated from this programme. Only about 40 hospitals in the country have nurses with an IPC diploma. Nurses of other hospitals can improve their IPC knowledge by attending the regional and national BulNoso Academia workshops.

34. Bulgaria has a mandatory continuing professional education programme for medical doctors and pharmacists. The NCIPD provides an annual one-week course on AMR, which is mandatory for medical doctors specialising in microbiology and voluntary for other medical specialisations. The NCIPD also provides different continuous education programmes in microbiology, including a course on antimicrobial chemotherapy. A new online course is under development with education on AMR and antibiotic stewardship for primary care providers and hospitals.

35. The Union of Pharmacists also has a web-based distance learning platform for continuing professional education of its members. There are plans to include a course on AMR; however, no funding has been available so far. A potential industrial sponsor has now been approached for funding as there is no public money available for this activity.

4.2.5 Public information related to AMR

36. The topic of AMR is currently vastly covered in the media, not only in connection with the European Antibiotic Awareness Day (EAAD) and the World Antibiotic Awareness Week in November, but also year-round. In the winter months, AMR is discussed in connection with influenza as many Bulgarians still believe that antibiotics are effective to treat influenza and other winter respiratory viruses (as confirmed in the Eurobarometer surveys). Since 2012, Bulgaria marked EAAD with various activities to promote prudent use of antibiotics. For 2018, the campaign was initially planned to target pharmacists, but the scope of activities had to be reduced due to the lack of resources. Nevertheless, at the time of the visit, a press conference was still planned for EAAD 2018. This lack of resources also meant less involvement in the EU-JAMRAI, including its communication work package.

37. The South-Eastern Europe Health Network (SEEHN) is an ongoing cooperation in the health sector in South-Eastern Europe, which is coordinated by WHO/Europe. Seven years ago, WHO/Europe appointed regional reference centres for different areas and Bulgaria took on board the coordination in the field of AMR. While some regional centres were very active, there has been little action on AMR. At the time of the visit, the WHO/Europe country office is very active for the preparation of the 2018 EAAD campaign and decided to take the lead and coordinate the activities in the country.

38. The campaigns on AMR are performed in collaboration with a public relations agency. The 2017 campaign was considered particularly successful and won a prize. Professional associations have been involved in the campaigns in the past, but could be more involved and in a more structured fashion. The NCPHA also works on public health campaigns but focuses mostly on non-communicable diseases. Local campaigns have not been performed by the Regional Health Inspectorates, but individual hospitals have organised local communication initiatives. Human resources, institutional support and limited funding remain the main obstacles to undertaking a fully-fledged national campaign. There has not been any formal evaluation of the campaigns; however, the Eurobarometer surveys can be used to estimate their impact regarding antibiotic use.

4.2.6 Marketing related issues

39. According to the BMA, independent - i.e. not supported by industry - information on medicines, including on antibiotics, is available from the BMA website. Advertisement of prescription-bound medicines to the public is forbidden in Bulgaria. Nevertheless, the pharmaceutical industry might influence antibiotic prescription practices via experts or opinion leaders. Physicians are not allowed to accept gifts from the pharmaceutical

industry and the number of free medication samples that can be handed out by the pharmaceutical industry to practitioners is limited and must be recorded [23].

40. One hospital reported receiving regular requests from the pharmaceutical industry to access staff to give information and presentations; however, no such presentation can be performed without the agreement of the hospital's medical director. Educational materials used by the pharmaceutical industry must be submitted to the BMA; however, there is no obligation for pharmaceutical companies to submit a list of the seminars that they have sponsored.

4.2.7 Conclusion on human health aspects of AMR

41. The current levels of AMR in Bulgaria are of concern. The levels of AMR in key indicator bacteria from humans, as reported to the European Antimicrobial Resistance Surveillance Network (EARS-Net), are high in comparison to most other EU/European Economic Area (EEA) countries. However, it is likely that the Bulgarian hospitals/laboratories that participate in EARS-Net represent a selected group resulting in selection bias. Data from the national AMR surveillance system BulSTAR give a better picture of the AMR situation in the country. Nevertheless, although data from BulSTAR show lower AMR proportions than data from EARS-Net, the reported AMR levels are high and show increasing AMR trends for specific bacterium-antimicrobial combinations.

42. Consumption of antibiotics in the community in Bulgaria, as reported to the European Surveillance of Antimicrobial Consumption Network (ESAC-Net), is at about the EU/EEA average, but the use of broad-spectrum antibiotics such as cephalosporins (oral) and fluoroquinolones is higher than in most other EU/EEA countries and is still increasing. In hospitals, consumption of antibiotics is below the EU/EEA average; however, Bulgaria reports the highest (>50%) proportion of all EU/EEA countries of use of broad-spectrum antibiotics in the hospital sector as well as a worrying increase in the consumption of last-line agents such as carbapenems and polymyxins.

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[23] In their response to the draft report the competent authority noted that under the Medicinal Products in Human Medicine Act, the Bulgarian Drug Agency is to keep and maintain a register of authorised medicinal products and registered medicinal products in Bulgaria, the data in the register being published on the Agency's official website: www.bda.bg. Medical professionals prescribing medicinal products may not claim or accept any material or other benefits from producers of medicinal products, marketing authorisation/registration certificate holders, medical sales agents and traders in medicinal products. In the event of promotional meetings, scientific congresses, symposia or other events for scientific purposes attended by medical specialists, sponsors or organisers may bear medical specialists' travel and accommodation expenses and the registration fees in the country in which the event takes place, with the exception of expenses to persons holding a public office within the meaning of Article 3 of the Conflict of Interest Prevention and Ascertainment Act, committee members referred to in Article 107(1), Article 259(1), Article 265(1) of the Medicinal Products in Human Medicine Act and members of the Supreme Council of Pharmacy. The Association of Research-Based Pharmaceutical Manufacturers in Bulgaria (ARPharM) has implemented the European Federation of Pharmaceutical Industries and Associations (EFPIA) Disclosure Code in the country. The EFPIA Disclosure Code requires all member companies to document and disclose certain transfers of value, directly or indirectly made to the benefit of health professionals or health organisations. Healthcare professionals, however, should agree to disclose their financial relationship with pharmaceutical companies.

43. There seem to be limited knowledge about AMR in healthcare professionals on all levels. This applies to authorities and stakeholders as well as to professional organisations/societies and medical doctors. This is underlined by a lack of understanding of the extent of the issue of AMR and of the urgency to effectively manage and control AMR in the country. In general, public health and communicable diseases seem to be low on the priority list, which results in under-resourcing and low staffing in many important areas, including the prevention and control of AMR. Many of the functions regarding surveillance and risk management of AMR still need to be established.

44. Independent (i.e. not sponsored), evidence-based national guidelines for the treatment of common infections, in the community and in hospitals, do not seem to be available in Bulgaria. As a consequence, clinicians mainly rely on their own clinical experience, on peers and on information provided by pharmaceutical companies when prescribing antibiotics. There also appear to be constraints in hospitals in terms of infrastructure (e.g. not enough single rooms to isolate patients with multidrug-resistant organisms (MDROs), in terms of resources (e.g. not enough use of alcohol-based hand rub for hand disinfection, and not enough screening of patients for carriage of MDROs), and a shortage in key healthcare personnel in various domains. The ageing workforce of specialists in the fields of AMR, antimicrobial consumption, healthcare-associated infections (HAIs) and IPC is also a concern [24].

45. The situation is even more challenged by the fact that the country is drained of academic healthcare professionals, who choose to move to work in other European countries. In addition, the restructuring and reorganisation, in recent years, of many functions within the healthcare system, including downscaling of several functions and significantly reduced financing, is a challenge for providing essential functions regarding communicable disease control within the different healthcare sectors and specifically challenges the establishment of new strategies on the prevention and control of AMR.

46. Bulgaria has high level of knowledge and skills within diagnostic microbiology and a well-established system for surveillance for AMR, for which improvements such as electronic reporting are planned. Still, too few clinical microbiology samples are taken in hospitals and there is lack of action in response to the results reported by clinical microbiology laboratories. Hospital IPC teams are in charge of prevention of HAIs and containment of AMR in hospitals, but in practice, it seems to be often difficult to establish a team with appropriate competences and receiving sufficient training. Assistance from the Regional Health Inspectorate is also often missing due to

[24] In their response to the draft report the competent authority noted that the National Council on Prices and Reimbursement of Medicinal Products in Bulgaria draws up pharmaceutical and therapy guidelines, which include criteria for assessing the effectiveness of the treatment and algorithms for treatment with medicinal products paid for with public funds that are agreed with the relevant council of experts by medical speciality or medical activity. Adherence to the approved pharmaceutical and therapy guidelines in Bulgaria and, where such are not available, to treatment standards and good medical practice in the European Union countries, is mandatory for all medicinal products on the Positive Medicine List. The Medical Supervision Executive Agency monitors compliance with the approved pharmaceutical and therapy guidelines and the assessment of the effectiveness of treatment.

underreporting of HAIs as well as understaffing of the Regional Health Inspectorates. This is partly due to the fact that reporting does not include AMR. In addition, there are no national guidelines on the screening for MDROs of certain patient populations or upon admission to hospitals or certain wards.

47. Other factors that contribute to the levels and trends of AMR include (a) limited multidisciplinary collaboration between clinicians, microbiologists, pharmacists and epidemiologists at hospital level, (b) division of responsibilities and limited collaboration between the different institutions, and (c) limited collaboration between the human and veterinary domains on prudent antibiotic use and AMR. In particular, Bulgaria does not have an Inter-sectoral One Health Coordinating Mechanism on AMR. Draft national action plans have been developed separately for animal health and for human health and are in various stages of development. The environmental aspects of the One Health approach are also not adequately covered in these plans.

48. On the other hand, there are several good programmes and initiatives, promoted by well-skilled individuals, organisations and institutions that can be used as the basis for future activities. Examples of such programmes and initiatives include:

- The national surveillance system for AMR (BulSTAR);
- The certification of clinical microbiology laboratories;
- The use of modern technologies such as molecular detection and typing at the national reference laboratory for AMR and the development of online training platforms;
- The extensive work on infection prevention and control done by the professional association the IPC society of Bulgaria (BulNoso);
- The initiatives to limit the sale of over-the-counter antimicrobial agents.

49. Bulgaria is at a critical point of time regarding its AMR situation. If appropriate measures are not taken and the current trends of AMR continue, it is likely that untreatable healthcare-associated infections, especially those caused by *Klebsiella pneumoniae* and *A. baumannii*, will become a reality, with an impact on the ability of hospitals to provide important medical services such as major surgical procedures, cancer treatment and intensive care.

4.3 VETERINARY AND ENVIRONMENTAL ASPECTS OF AMR

4.3.1 Monitoring of AMR in animals and food, including relevant laboratory capacity

50. Bulgaria has nominated the National Diagnostic Veterinary Institute as national reference laboratory (NRL) for AMR. Aside from the relevant proficiency testing as part of the EU NRLs coordinated activities, the NRL carries out the required monitoring of AMR in zoonotic and commensal bacteria in food producing animals and food, and

reports the results to EFSA, in accordance with the requirements of Decision 2013/652/EU (see section 2).

51. As part of the National Diagnostic Veterinary Institute, there is a small network of two official laboratories carrying out diagnostic and susceptibility testing for veterinary pathogens. These laboratories receive post mortem samples for diagnostic investigations including sensitivity testing. The throughput of samples received and tested by these government laboratories was reported to be very small for most of the livestock species and particularly low for cattle and poultry.

52. The levels of AMR in zoonotic and commensal bacteria are high in Bulgaria compared to some other Member States. For example, the level of resistance to erythromycin in *Campylobacter jejuni* from broiler flocks was the highest in Europe in 2016 (10.9% compared to an EU average of 1.3%) [25]. These results are of concern, since erythromycin is a last resort antimicrobial for the treatment of Campylobacteriosis in people, including children.

53. During the visit, AMR issues were reported or observed both in veterinary pathogens and in bacteria of importance for human health, e.g. pathogenic *Escherichia coli* and methicillin-resistant *Staphylococcus aureus* (MRSA) in companion animals, respectively. However, there was no evidence of any action taken by the competent authority to minimise and control the potential impact of these findings for human or animal health (e.g. expert veterinary advice given to farmers and veterinarians on control options of resistant veterinary pathogens, follow-up investigations or advice and information to owners on the potential risk of zoonotic organisms such as MRSA). A lack of formal communication of AMR issues to human health authorities was noted by the Commission team.

54. A diagnostic service carried out by the private sector is also available and used by the industry and the companion animal sector. However, access to these data is currently not available to the authorities and there is lack of collaboration between the private sector and government laboratories in sharing and analysing such data.

55. The Commission team noted several research efforts [26] and international collaborations to further develop the understanding and knowledge of AMR in zoonotic and commensal organisms in Bulgaria. However, there is limited use of the resulting data to inform policy and help to develop the national action plan to control AMR.

56. Available AMR surveillance data are not holistically and systematically analysed or presented from the perspective of its implications for human or animal health. Many useful data are only made available through academic/scientific publications. The collation and analysis of the available data (including from private laboratories if possible) have been key tools in other Member States for prioritising actions, follow-up and other interventions to limit the impact of AMR on human and animal health.

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25 https://ecdc.europa.eu/sites/portal/files/documents/AMR-zoonotic-bacteria-humans-animals-food-2016_Rev3.pdf

26 http://www.effort-against-amr.eu/

4.3.2 Monitoring the use of antimicrobials in animals

57. The European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) report published in October 2018 [27] shows an overall increase of 27% in the total consumption of antimicrobial VMPs in Bulgaria in 2016 (compared to 2015): 155.3 mg/ PCU (population correction unit), within a range of 2.9 to 453.4 mg/PCU for the other countries contributing data to ESVAC. BFSA explained to the Commission team that this 27% increase might represent incomplete reporting of sales and consumption in previous years, rather than an actual increase in antimicrobial consumption in 2016. The ESVAC report notes that sales of 3rd and 4th generation cephalosporins in Bulgaria represented 0.1% of total sales (mg/PCU) in 2016.

58. The Commission team was informed that the data reported to ESVAC do not currently take account of antimicrobials brought into the country by veterinarians (under the cascade) or the use of human medicines in animals. The veterinarians met indicated that the quantities and type of antimicrobials from these sources is significant and helps to ensure an adequate range and availability of antimicrobials for use in animals. Other Member States with similar issues have developed specific procedures and national rules to try and ensure that it is known what antimicrobials are actually being used in animals and the quantities being supplied from neighbouring countries. The implementation of similar measures could be considered in Bulgaria. As a key indicator for the success of any national AMR action plan in reducing antimicrobial use or changing behaviour concerning the prescribing and choice of antimicrobials, it would be important to increase the reliability and completeness of this data reporting to ESVAC.

59. A small animal veterinary practitioner met by the Commission team stated that it is a regular occurrence in Bulgaria that a particular antimicrobial is not effective and there is a need either to increase the dose administered or to switch to another product (sometimes containing the same active substance). It was stated that such reported cases of lack of efficacy are reported to the authorities in line with applicable pharmacovigilance guidance.

4.3.3 Environmental monitoring of antimicrobials and AMR

60. The Ministry of Environment and Water is involved in the monitoring of substances, including macrolides under Commission Implementing Decision (EU) 2015/495 establishing a watch list of substances for Union-wide monitoring in the field of water policy. The monitoring has already been performed and the results were reported to the European Commission in December 2017. It was stated that there are currently no other particular actions under way in this Ministry concerning AMR.

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27 https://www.ema.europa.eu/documents/report/sales-veterinary-antimicrobial-agents-30-european-countries-2016-trends-2010-2016-eighth-esvac_en.pdf.

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

4.3.4.1 Sector specific targets for reducing, refining or replacing antimicrobial use

61. The Commission team was not informed of any sector specific targets currently applicable in Bulgaria to reduce, refine or replace antimicrobial use in animals. The pig farm visited had recently switched from using tiamulin in medicated feed for weaning piglets' enteritis to using colistin. It was stated that this change had been recommended by some academic experts. The dairy farm visited had recently purchased oral powders containing colistin. The attending veterinarian stated that this was upon the recommendation of the supplying VMP wholesaler. The Commission team noted a lack of awareness among the veterinarians and officials met concerning any particular issues related to AMR and the use of colistin in animals or the scientific advices issued by EMA on this subject [28].

62. A possible future initiative to develop an e-traceability system from the prescribing of antimicrobials through to their administration to individual animals is under consideration by the authorities and stakeholders. It was stated that this would provide improved data on how antimicrobials are supplied and used and the possible application of penalties if applicable rules or legislation are infringed.

63. The Commission team was not informed of any benchmarking systems currently in place in Bulgaria concerning antimicrobial prescribing and use by veterinarians and use at farm level. Some other Member States have found such schemes useful as a way of measuring antimicrobial use and prescribing, incentivising reduced and more prudent use and in some cases acting as a tool to guide official controls or advisory actions.

4.3.4.2 Availability of veterinary antimicrobials and veterinary care

64. Stakeholders met by the Commission team stated that farmers in Bulgaria can quite easily source antimicrobials for use in their animals without a prescription. It was stated that in some cases veterinarians issue prescriptions without having examined the animals and that BFSA are aware of such cases. Since human antimicrobials are cheaper and more available than comparable veterinary products, pet owners often source such human products from pharmacists and initiate treatments without a veterinary examination, due to the costs of a veterinary consultation. It was stated that the most common human antimicrobial used in pets is doxycycline, for which there is no equivalent veterinary product in Bulgaria and that in most cases this antimicrobial is administered blindly without any examination or diagnostic tests being performed.

65. There was a permanent private veterinary presence on the pig and dairy farms visited. This is apparently a standard characteristic of large farms in Bulgaria in order to enable these veterinarians to identify and react to diseases as they appear (potentially reducing the need for prophylactic treatments) and avoid the need for farmers to decide when to

[28] https://www.ema.europa.eu/veterinary-regulatory/overview/antimicrobial-resistance/advice-impacts-using-antimicrobials-animals.

initiate treatments and administer antimicrobials themselves. This places the veterinarian in a strong position to act as a gatekeeper for the use and prudent use of antimicrobials, which has been a key element in many Member States with successful AMR policies.

66. Nevertheless, the Commission team considered that there is an urgent need to raise veterinarians' knowledge about AMR and the prudent use of antimicrobials. The draft veterinary-food national AMR action plan correctly identifies this as an issue which the BVU and universities should also be involved in addressing.

67. Although the small animal and poultry veterinarians met were quite aware of AMR and prudent use principles, the other veterinarians met (both officials and practising veterinarians) displayed a very limited knowledge of relevant issues. The Commission team was informed that this is also characteristic of recent veterinary graduates in Bulgaria and that the current veterinary curriculum does not adequately address AMR issues. Continuous professional development by veterinarians is not currently required in Bulgaria as it is in some other Member States and practising veterinarians met commented on the limited availability of relevant training opportunities in Bulgaria on AMR (attending courses abroad instead) and a lack of relevant guidance either from the national authorities or veterinary professional organisations.

68. Unlike most other Member States, Bulgaria has not put in place any particular restrictions which could support the prudent use of antimicrobials. The adoption of national measures could be a useful tool to discourage use of the most important antimicrobials for human medicine (e.g. one veterinarian informed the Commission team that meropenem could be easily sourced in Bulgaria and used in animals). Clear requirements relating to the use of critically important antimicrobials (CIAs) have helped to substantially reduce their use in animals in various Member States, with national rules often requiring a diagnostic and antimicrobial sensitivity test to be performed to justify their use in animals and to demonstrate the lack of effective alternative antimicrobial treatments. The enforcement of such national measures has been an effective means to bring about rapid changes in the use of CIAs in animals in some other Member States.

69. Off-label use of antimicrobials in animals will be more comprehensively regulated in the upcoming EU Regulation on VMPs [29]. Veterinarians informed the Commission team that they regularly deviate from the SPC to use much higher doses as otherwise the antimicrobial is quite ineffective at the recommended dose. Some Member States currently allow for this deviation from the recommended dose, for example for the use of older penicillin products.

70. According to the small animal veterinary practitioners met, deviating from the BVU's Good Veterinary Practice (e.g. changing the duration of antimicrobial treatment and not using antimicrobials peri-operatively) can leave the veterinarians open to sanctions by the Commission for Control and Professional Ethics of the BVU or oblige them to defend their actions in court cases taken by the animal owner and with nominated expert

[29] https://ec.europa.eu/health/veterinary-use_en

witnesses who might not be aware of the latest principles concerning the reduced and more prudent use of antimicrobials in animals. Penalties that can be applied by the Commission include suspending a veterinarian's registration for 3 months, fines of 3 000 leva and inspections of their veterinary practice. In court cases a veterinarian could lose the right to practise for 5 years.

71. For this reason it was stated that some small animal veterinary practitioners are afraid to discharge an animal from their clinic without a 6-10 day course of antimicrobials. Veterinarians met also encouraged the Bulgarian authorities to ensure that expert witnesses nominated for such court cases should be cognisant of more recent developments in AMR and prudent use.

72. The Commission team noted that BVU's Good Veterinary Practice guide from 2008 could be usefully updated to take account of latest developments concerning AMR and prudent use. Some of the small animal veterinary practitioners met stated that BVU should issue clear guidance on the AMR and prudent use issue implementing good practices identified in other Member States and that such guidance should be binding.

73. The Commission team noted that there is a lack of sector specific guidance or supporting tools currently available, publicised or used in Bulgaria to help veterinarians reach appropriate decisions about antimicrobial use. There are many useful examples available in published reports on this issue [30], including on infection prevention and control also in small animal veterinary practices.

4.3.4.3 Reducing the need for veterinary antimicrobials

74. The Commission team was not informed of any official initiatives to reduce the need for veterinary antimicrobials to be used. On the pig and dairy farms visited and in meetings with the attending veterinarians the Commission team was not informed of any specific actions which had been taken to reduce the use of antimicrobials. The dairy farm visited routinely used antimicrobial dry cow therapy. The veterinarian stated that he chose the product as being effective based on his previous clinical experience and the Commission team did not see any documentation to support the selection of the antimicrobial dry cow product used. The veterinarian stated that in the past they had used oxytetracycline to treat mastitis but that this was not very effective and so they now used enrofloxacin. Ceftiofur was used routinely to treat cows with endometritis and retained placenta on this farm and marbofloxacin was used to treat acute enteritis and mastitis. The veterinarian stated that milk from animals treated with antimicrobials is not given to younger animals on the farm but is instead thrown into an effluent lagoon on the farm.

75. The Commission team was not informed of any particular restrictions applying in Bulgaria to the use of veterinary antimicrobials, including CIAs and colistin. Most of the practising veterinarians, farmers and official inspectors met by the Commission team had a low awareness of what constituted CIAs in veterinary medicine or any particular

30 http://ec.europa.eu/food/audits-analysis/overview_reports/details.cfm?rep_id=121

AMR aspects related to the use of colistin in animals, which has been the subject of various EMA advices, including on measures to reduce the use of colistin in animals [31].

76. The Commission team met with a representative of a large integrated poultry breeding company which stated that it had reduced its total antibiotic use in recent years by over 50% through the avoidance of prophylactic treatments and improvement of biosecurity etc.

77. The small animal veterinary practitioners met by the Commission team informed that in Bulgaria human-authorised antimicrobials are often used in companion animals since such products are cheaper and more available than equivalent veterinary antimicrobials. A BFSA inspector in charge of VMP controls confirmed that the use of human antimicrobials in animals is permitted in Bulgaria if no analogous veterinary product is available and their use is justified to relieve the suffering of the animal. There are no special rules restricting the use of human antimicrobials such as meropenem in animals. In the small animal veterinary practice visited it was stated that they aim to reduce the peri-operative use of antimicrobials for routine surgeries, as is successfully applied in some other Member States.

78. One small animal veterinary practitioner, who also acts as a VMP wholesaler for a group of small animal clinics, stated that the fee to register VMPs on the Bulgarian market is very expensive and estimated that they ordered 30% of their veterinary products via online pharmacies based in Austria or Greece. It was stated that a veterinary antimicrobial such as verofloxacin is 30% more expensive in Bulgaria than in Austria and this also encourages pet owners to source human antimicrobials directly from pharmacies to treat their animals. Various stakeholders mentioned that veterinarians are financially dependent on farmers and pet owners and this affects the prescribing of antimicrobials upon their request.

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

79. Apart from the publication of the EU 2015 guidelines on the prudent use of antimicrobials in veterinary medicine on the BFSA website and the organisation in 2016 of a workshop with representatives of the BVU and Association of Producers, Importers and Traders of veterinary medicinal products, the Commission team was informed of no other specific communication and awareness activities on AMR and the prudent use of antimicrobials in animals. One of the small animal veterinary practitioners met by the Commission team stated that they were not aware of any communication, awareness or training events on AMR or prudent use organised by the authorities or BVU.

80. Stakeholders met by the Commission team stated that in Bulgaria everyone feels quite free to administer antimicrobials as they wish and that if the AMR issue is left to veterinarians alone there will be no major improvements since they are trapped by

[31] https://www.ema.europa.eu/veterinary-regulatory/overview/antimicrobial-resistance/advice-impacts-using-antimicrobials-animals.

market conditions and animal owners who demand rapid and cheap treatments. It was stated that many small animal veterinary practitioners do not believe that their daily work greatly affects the issue of AMR and that the greatest issues regarding over use or imprudent use of antimicrobials are considered to be in the farm animal or human health sectors.

81. The draft veterinary/food national action plan on AMR includes a strategic objective of raising public awareness and knowledge on the risks of development of AMR through effective communication, education and training. Various strategic actions and activities are proposed in the draft action plan under this strategic objective.

4.3.6 Conclusion on veterinary and environmental aspects of AMR

82. There was a generally very low awareness and motivation to act concerning AMR and the prudent use of antimicrobials in animals among most of the stakeholders (farmers, veterinarians, etc.) and officials met by the Commission team. Very few initiatives have been taken by the Bulgarian authorities to date on these issues.

83. Little use is made of existing veterinary/food AMR surveillance data, either to formally discuss it with human health colleagues or to warn veterinarians, farmers or pet owners when bacteria with human health implications such as MRSA are detected in their animals or premises. Many pet/companion animals are treated with human authorised antimicrobials since these are generally cheaper and more available than comparable veterinary products.

84. Apart from the compulsory monitoring of water for substances such as macrolide antibiotics required under EU legislation, no further actions on environmental aspects of AMR are under way or planned, which is quite similar to some other Member States.

5 OVERALL CONCLUSION

There are numerous gaps and weaknesses in the approach towards tackling AMR in Bulgaria, both in the veterinary and human health domains, which compare poorly with the situation in other Member States. There is in particular a significant lack of communication and collaboration between the veterinary, human health and environmental authorities in a One Health perspective. There is no Inter-sectoral One Health Coordinating Mechanism on AMR, and draft national action plans for animal health and for human health, which are in various stages of development, have been developed separately.

In the human area, the current levels of AMR in Bulgaria are of concern. There seems to be limited knowledge about AMR in healthcare professionals on all levels. This is underlined by a lack of understanding of the extent of the issue of AMR and of the urgency to effectively manage and control AMR in the country. There also appear to be constraints in hospitals in terms of infrastructure, resources and a shortage in key healthcare personnel in various domains. If appropriate measures are not taken and the current trends of AMR continue, it is likely that untreatable healthcare-associated infections will become a reality, with an impact on the ability of hospitals to provide important medical services such as major surgical procedures, cancer treatment and intensive care.

In the veterinary area, awareness concerning AMR matters is generally very low and few effective initiatives have been taken by the national authorities to date, which stated that this was due to the existence of other pressing work priorities, such as dealing with cases of African Swine Fever.

6 CONSIDERATIONS FOR POSSIBLE FUTURE ACTIONS

6.1.1 Human aspects of AMR

Concerning human health and based on the visit's observations and conclusions, the ECDC team identified the following points which may be useful to be taken in consideration by the relevant competent authorities in further developing and implementing the national AMR strategy and action plan:

- Establish a high-level inter-sectoral and multi-disciplinary coordination mechanism including representatives from the animal health, human health and environmental sectors.
- Merge and further develop the current drafts of the veterinary AMR action plan and the human AMR action plan (i.e. national programme for rational use of antibiotics and antibiotic resistance surveillance) into one single “One Health” National Action Plan for AMR as the first task of the inter-sectoral coordination mechanism.
- Involve all national stakeholders such as Ministries of Health, of Agriculture and of the Environment, the BFSA, the NCIPD, professional associations such as BulNoso, professional medical and pharmacy organisations and unions as well as other relevant stakeholders in the consultations on this national action plan.

- Finalise the National Action Plan on infection prevention and control.
- Improve communication and collaboration between stakeholders working on AMR and infection prevention and control in the human health sector and establish regular meetings between the Ministry of Health, the NCIPD, professional associations and other relevant stakeholders to work on AMR.
- Ensure that political support by all involved ministries and sufficient funding for the actions proposed in the national action plans is available.
- Develop independent (i.e. not sponsored) national guidelines:
    - For surgical prophylaxis;
    - For the treatment of common infections in the community/ambulatory care;
    - For the treatment of common infections in hospitals;
    - For screening of specific patient categories for MDROs.

  These guidelines should take into account national AMR patterns, but should be based on the principles of antimicrobial stewardship and prudent use of antibiotics. All stakeholders should be consulted in the development and regular update of these guidelines.
- Make sure that the hand hygiene campaign planned by BulNoso (based on the model proposed by the World Health Organisation (WHO) to promote the use of alcohol-based hand rub in healthcare) is conducted as a national hand hygiene campaign, supported by the Ministries and involving all stakeholders.
- Develop a long-term communication strategy on prudent use of antibiotics that includes the NCIPD, the Ministry for Health, national medical and other professional organisations and communication experts as well as ECDC and the WHO Country Office with consideration of:
    - Inclusion of low-cost initiatives such as social media campaigns with support of stakeholders;
    - involvement of health stakeholders, such as BulNoso or the patient safety association as well as other institutions in the planning phase;
    - increased use of materials developed by WHO/Europe and ECDC, which are available also in Bulgarian;
    - exploration of the use of the e-bug material in Bulgaria to target young students, as well as designation of a national focal point for e-Bug;
    - addition of an element of evaluation to all campaign efforts;
    - ensuring that communication efforts are consistent and developed through a number of years;
    - use of the E-learning module on AMR to train the trainers at local level and improve awareness among health professionals.

- Increase the general knowledge about AMR, hospital hygiene and prudent use of antibiotics among all groups of healthcare professionals at all levels, to better understand the importance and consequences of AMR.
- Strengthen the infection prevention and control teams in hospitals and make sure that they have access to AMR and antimicrobial consumption data and are also involved in antimicrobial stewardship activities in hospitals. Sharing of good practices among hospitals should be encouraged.
- Explore how revision of clinical pathways could be used to strengthen prudent use of antimicrobials, increasing microbiological sampling and diagnosis, and prevention of HAIs.
- Revise the ordinance for mandatory reportable diseases to include detections of MDROs of public health importance such as carbapenem-resistant Enterobacteriaceae, carbapenem-resistant *A. baumannii*, VRE, MRSA, as well as any detection of pandrug-resistant microorganisms.
- Increase the participation of laboratories in EARS-Net to improve the coverage of AMR surveillance in Bulgaria and the representativeness of data from Bulgaria in EARS-Net. The transition of BulSTAR from aggregated to electronic data should serve as the basis for this improvement of reporting to EARS-Net.
- Use the data from BulSTAR to provide analysis on AMR trends at regional/local level.
- Provide analysis and reports on antibiotic consumption at regional/local level based on available data.
- Collect data from hospital pharmacies at national level to produce reports on antibiotic use and its appropriateness.
- Participate in EU Joint Actions such as on AMR and HAIs (EU-JAMRAI) and on One Health (One Health EJP).

The above-mentioned actions could be implemented in the short and medium term. A longer-term sustainable situation will require an upgrade of the hospital and healthcare infrastructure, with proper isolation facilities and sufficient numbers of trained staff, and more resources provided to the healthcare sector.

6.1.2 Veterinary and environmental aspects of AMR

Concerning veterinary and environmental aspects the Commission team identified the following points which may be useful to be taken into consideration by the relevant competent authorities in further developing and implementing the national AMR strategy and action plan:

- Ensure greater effective cooperation and collaboration between authorities and stakeholders covering the human health, veterinary and environmental sectors to

promote an effective One Health approach to tackling AMR in practice and in finalising and implementing in the near future a national AMR action plan.

- Take steps to encourage the industry, professional associations and other relevant stakeholders to participate in the development of the national AMR action plan and to secure a commitment on their part to contribute to the successful implementation of relevant actions.
- Raise awareness and understanding of the AMR issue among farmers, veterinarians, government authorities, animal and pet owners and the general public, including how AMR may spread between and among people, animals and the environment, and what can be done to control it.
- Work with the livestock industry and the veterinary profession (including universities) to promote best practice on reduced and prudent use of antibiotics, through compulsory rules if considered necessary, as well as on animal husbandry, infection prevention and control.
- Incorporate aspects relevant to AMR and prudent use into routine official inspections of farms, veterinary practices, feed mills producing medicated feed, pharmacies, VMP retailers and wholesalers.
- Take specific actions to monitor, control and reduce the use of CIAs and colistin in animals.
- Further develop and improve surveillance schemes that collect data on antimicrobial use and AMR in animals that can be used to inform treatment and prescribing practices, detect the emergence of AMR threats, evaluate trends, and take action to minimise and control the impact of AMR for animal and human health.

7 CLOSING MEETING

The ECDC and Commission teams presented the main findings and preliminary conclusions of the visit to the competent authorities in a closing meeting held on 19 October 2018.

ANNEX 1 – LEGAL REFERENCES

Legal Reference	Official Journal	Title
Dir. 90/167/EEC	OJ L 92, 7.4.1990, p. 42-48	Council Directive 90/167/EEC of 26 March 1990 laying down the conditions governing the preparation, placing on the market and use of medicated feedingstuffs in the Community
Dir. 96/23/EC	OJ L 125, 23.5.1996, p. 10-32	Council Directive 96/23/EC of 29 April 1996 on measures to monitor certain substances and residues thereof in live animals and animal products and repealing Directives 85/358/EEC and 86/469/EEC and Decisions 89/187/EEC and 91/664/EEC
Dir. 2008/105/EC	OJ L 348, 24.12.2008, p. 84-97	Directive 2008/105/EC of the European Parliament and of the Council of 16 December 2008 on environmental quality standards in the field of water policy, amending and subsequently repealing Council Directives 82/176/EEC, 83/513/EEC, 84/156/EEC, 84/491/EEC, 86/280/EEC and amending Directive 2000/60/EC of the European Parliament and of the Council
Dir. 2001/82/EC	OJ L 311, 28.11.2001, p. 1-66	Directive 2001/82/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to veterinary medicinal products
Dec. 2013/652/EU	OJ L 303, 14.11.2013, p. 26-39	2013/652/EU: Commission Implementing Decision of 12 November 2013 on the monitoring and reporting of antimicrobial resistance in zoonotic and commensal bacteria
Dec. 2015/495/EU	OJ L 78, 24.3.2015, p. 40–42	Commission Implementing Decision (EU) 2015/495 of 20 March 2015 establishing a watch list of substances for Union-wide monitoring in the field of water policy pursuant to Directive 2008/105/EC of the European Parliament and of the Council
Reg. 851/2004	OJ L 142, 30.4.2004, p. 1-11	Regulation (EC) No 851/2004 of the European Parliament and of the Council of 21 april 2004 establishing a European Centre for disease prevention and control

Council Rec. 2002/77/EC	Official Journal L 034 , 05/02/2002 P. 0013 - 0016	Council Recommendation of 15 November 2001 on the prudent use of antimicrobial agents in human medicine