

EAHP Position Paper on Antimicrobial Resistance (AMR)

making the difference in medication

- prudent use of Antimicrobial Drugs through Antibiotic Stewardship (ABS) to ensure efficient therapy for patients with life threatening infections

Antibiotics and other antimicrobial drugs save lives. Scientific evidence has become widespread in policy and general knowledge: inadequate use and overuse of antimicrobials in human medicine, veterinary medicine and intensive livestock farming as well as pharmaceuticals in the environment endanger the potency and efficacy of antimicrobial agents. Development and increase of antimicrobial resistance (AMR) put patients with life threatening infections at risk of therapeutic insufficiency.^{1,2} In addition, the lack of newly developed antibiotics worsens the situation.

To maintain the efficacy of antimicrobial drugs and to prevent further spread of AMR, EAHP demands an interprofessional approach. Hospital Pharmacists in Europe are ready to contribute and promote the prudent use of antimicrobial drugs through the enforcement of ABS. To improve patient outcomes proactive steps need to be taken. Consequently,

EAHP calls on national governments and health system managers to utilise the specialised background and knowledge of the hospital pharmacists in multi-professional antibiotic stewardship teams.

EAHP recommends universal application of infection prevention and control measures by ECDC and WHO among healthcare professionals.

EAHP strongly supports regulatory oversight and proper implementation of measures in the veterinary and agriculture sectors on European, national and local level.

EAHP urges increased investment to support the development of innovative proposals and the encouragement of practice based research projects to investigate new fields of infectious disease control such as immunotherapy and to optimise the cost-effectiveness of systems for surveillance on antibiotic use and resistance.

EAHP urges governments to make arrangements that essential antibiotics will be maintained on the market with contingency stock level arrangements and alternative production by hospital pharmacists enabled where necessary

1 STRENGTHENING OF ANTIMICROBIAL/ANTIBIOTIC STEWARDSHIP (ABS) IN HUMAN MEDICINE

1.1 DEVELOPMENT AND DEFINITION OF ANTIMICROBIAL/ANTIBIOTIC STEWARDSHIP (ABS)

In PubMed the first article using the term “Antimicrobial Stewardship” in a title or abstract was in the 1997 *Guidelines for the Prevention of Antimicrobial Resistance in Hospitals* published by the Society for Healthcare Epidemiology of America (SHEA) together with the Infectious Diseases Society of America

(IDSA)³. Over the following decade, only very few publications using this term in a title or abstract can be found in PubMed. In 2007 SHEA and IDSA published the *Guidelines for developing an institutional program to enhance antimicrobial stewardship*.⁴ ABS was described as an activity that includes appropriate selection, dosing, route, and duration of antimicrobial therapy. The primary goal of ABS is to optimize clinical outcomes while minimizing unintended consequences of antimicrobial use. Core members of a multidisciplinary ABS team include an infectious diseases physician and a clinical pharmacist with infectious diseases training, with the inclusion of a clinical microbiologist and further specialists being optimal.

The first European adoption of the IDSA Guidelines based on a new evaluation of the literature including European publications was performed in 2013. Published in German by an interdisciplinary working group from Austria, Germany and Switzerland⁵ it was later transferred into English⁶ to reach a wider audience in Europe.

In the following years, the number of publications using the terms "antimicrobial stewardship" or "antibiotic stewardship" in a title or abstract increased rapidly to over 740 in 2017⁷. 30 Years after the first publication, the concept of antibiotic stewardship has reached clinic practise and science.

1.2 NEED OF FURTHER IMPLEMENTATION OF ANTIBIOTIC STEWARDSHIP PROGRAMMES

ABS is still far away from being routine in European hospitals. This contrasts with the scientific results of efficient reduction of antibiotic overuse, positive contributions to resistance development and even cost savings through ABS⁸. The European Centre for Disease Prevention and Control (ECDC) also supports the strengthening of the fight AMR i.e. through an ABS toolkit with one particular section identifying ABS as a role requiring hospital pharmacists involvement.⁹

The EU Commission strongly supports ABS as an important tool in their publications e.g. EU Guidelines for the prudent use of antimicrobials in human health.¹⁰ Besides the positive effects on patient treatment and sustainability of antibiotic therapy there is also a cost benefit described in the literature¹¹.

FIP mentions as one point the important role of pharmacists in their statement of policy "control of AMR"¹², recommending that pharmacists *conduct and translate research on all facets of AMR, including but not limited to biomedical, clinical, socio-behavioural, policy, diagnostics and antimicrobial medicines discovery for the optimal management of infections in the context of AMR and antimicrobial stewardship in the One Health approach*. This especially applies to Hospital Pharmacists in Europe and elsewhere.

A recent editorial of the European Journal of Hospital Pharmacy stated: *First we need to take personal responsibility and ask: 'What am I or my pharmacy doing to improve control of antimicrobials?' Second there is a need to ensure that an up-to-date antimicrobial policy is available and implemented, with pharmacists playing their part on the policy committee*.¹³

EAHP calls on national governments and health system managers to utilise the specialised background and knowledge of the Hospital Pharmacists in multi-professional antibiotic stewardship teams.

2 FURTHER DEVELOPMENT OF PROPHYLACTIC MEASURES LIKE VACCINATION AND HYGIENE

The efforts of prophylaxis like vaccination and hygiene are additional supportive, important and need to be further enhanced. Prevention of infectious diseases should be strengthened by integrating

vaccination planning developed for the fight against AMR.^{14,15} Similarly existing toolkits such as the one for healthcare professionals in hospitals and other healthcare settings of ECDC, to which EAHP contributed from the perspective of the Hospital Pharmacist, and hand hygiene as the single most important prophylactic measure need to be further prompted.^{16,17}

EAHP recommends universal application of infection prevention and control measures by ECDC and WHO among healthcare professionals.

3 ADEQUATE USE OF ANTIMICROBIALS IN VETERINARY MEDICINE AND INTENSIVE LIVESTOCK FARMING

There is strong evidence that the use of antimicrobial drugs in agriculture and aquaculture also induce AMR in human pathogenic bacteria. The consumption of antimicrobials by animals in the EU is at least double than for humans in tonnes of active substances (8,1 vs. 3,8 t), and even significantly higher when comparing the biomass (147 vs. 124 mg/kg)¹⁸.

The EU Commission has taken significant measures in the veterinary sector and defined guidelines that address the need for preventive measures on European, national and local level.¹⁹

EAHP strongly supports regulatory oversight and proper implementation of measures in the veterinary and agriculture sectors on European, national and local level.

4 LACK OF NEWLY DEVELOPED ANTIBIOTICS AND UNIVERSAL ACCESS TO ESSENTIAL ANTIBIOTICS

Due to increase of resistance such as for instance carbapenem resistance in southern and eastern Europe specific funding actions are necessary for the future benefit the patients.²⁰ In 2017, the WHO stated:

- *The current clinical pipeline is insufficient against pathogens on the WHO priority pathogens list and TB,*
- *More innovative approaches are required, but there are scientific challenges and;*
- *More work is required to fill the pipeline.*²¹

Despite the commitments of the European Commission included in the One Health Action Plan in relation to the support of research and developments further incentives are needed.

EAHP **urges** increased investment to support the development of innovative proposals and the encouragement of practice based research projects to investigate new fields of infectious disease control such as immunotherapy and to optimise the cost-effectiveness of systems for surveillance on antibiotic use and resistance.²²

In addition to the development of new antibiotics the universal access to old antibiotics that are being utilised in new ways needs to be ensured. Studies that gather further information on this should be supported.²³ Medicines shortages of antimicrobial drugs endangers their prudent use and therefore should be avoided.

EAHP urges governments to make arrangements that essential antibiotics will be maintained on the market with contingency stock level arrangements and alternative production by hospital pharmacists enabled where necessary.

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- ¹ Council conclusions on the next steps under a One Health approach to combat antimicrobial resistance (June 2016). Available at (12.04.2018): <http://www.consilium.europa.eu/en/press/press-releases/2016/06/17/epsco-conclusions-antimicrobial-resistance/>
- ² A European One Health Action Plan against Antimicrobial Resistance (AMR). Available at (12.04.2018): https://ec.europa.eu/health/amr/sites/amr/files/amr_action_plan_2017_en.pdf
- ³ Shlaes DM, Gerding DN, John JF Jr, Craig WA, Bornstein DL, Duncan RA, Eckman MR, Farrer WE, Greene WH, Lorian V, Levy S, McGowan JE Jr, Paul SM, Ruskin J, Tenover FC, Watanakunakorn C. Society for Healthcare Epidemiology of America and Infectious Diseases Society of America Joint Committee on the Prevention of Antimicrobial Resistance: guidelines for the prevention of antimicrobial resistance in hospitals. *Infect Control Hosp Epidemiol.* 1997 Apr;18(4):275-91.
- ⁴ Dellit TH, Owens RC, McGowan JE, et al. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. *Clin Infect Dis* 2007; 44:159–77.
- ⁵ de With K, Allerberger F, Amann S et al.: Strategien zur Sicherung rationaler Antibiotika-Anwendung im Krankenhaus S3-Leitlinie, AWMF-Registernummer 092/001; 15. Dezember 2013. Available at (25.02.2018): www.awmf.org/uploads/tx_szleitlinien/092-001_S3_Antibiotika_Anwendung_im_Krankenhaus_2013-verlaengert.pdf
- ⁶ de With K, Allerberger F, Amann S, et al. Strategies to enhance rational use of antibiotics in hospital: a guideline by the German Society for Infectious Diseases. *Infection* 2016;44:395–439. doi:10.1007/s15010-016-0885-z
- ⁷ Results by year. Available at (11.04.2018): [www.ncbi.nlm.nih.gov/pubmed?term=\(%22antimicrobial%20stewardship%22%5BTitle%2FAbstract%5D%20OR%20%22antibiotic%20stewardship%22%5BTitle%2FAbstract%5D\)](http://www.ncbi.nlm.nih.gov/pubmed?term=(%22antimicrobial%20stewardship%22%5BTitle%2FAbstract%5D%20OR%20%22antibiotic%20stewardship%22%5BTitle%2FAbstract%5D))
- ⁸ Wickens, H.J., et al., The increasing role of pharmacists in antimicrobial stewardship in English hospitals. *Journal of Antimicrobial Chemotherapy*, 2013. 68(11): p. 2675-2681
- ⁹ Available at (10.04.2018): <https://ecdc.europa.eu/en/news-events/european-antibiotic-awareness-day-new-website-new-online-resources> and <https://antibiotic.ecdc.europa.eu/en/get-informed/key-messages/key-messages-professionals-hospitals-and-other-healthcare-settings/key-7>
- ¹⁰ EU Guidelines for the prudent use of antimicrobials in human health (C/2017/4326). Available at (12.04.2018): http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=uriserv:OJ.C_.2017.212.01.0001.01.ENG&toc=OJ:C:2017:212:TOC
- ¹¹ van Lent-Evers, Impact of goal oriented and model based clinical pharmacokinetic dosing of aminoglycosides on clinical outcome: a cost-effectiveness analysis, *Therapeutic Drug Monitoring* 1999; 21: 63-73
- ¹² International Pharmaceutical Federation. FIP Statement of Policy - control of antimicrobial resistance (AMR). The Hague: FIP, 2017. Available at (25.02.2018): http://www.fip.org/www/uploads/database_file.php?id=386
- ¹³ Wiffen P Apocalypse: the end of antibiotics? *Eur J Hosp Pharm* 2018;25:1.
- ¹⁴ Vaccines Europe priorities for vaccination policies in Europe (June 2017). Available at (12.04.2018): http://www.vaccineseuropa.eu/wp-content/uploads/2017/06/VE-paper_priorities_vaccination_policy-22-05-2017.pdf
- ¹⁵ The review on Antimicrobial Resistance (Chaired by Jim O'Neill) (February 2016). Available at (12.04.2018): https://amr-review.org/sites/default/files/Vaccines%20and%20alternatives_v4_LR.pdf
- ¹⁶ ECDC (European Centre for Disease Prevention and Control) Toolkit for healthcare professionals in hospitals and other healthcare settings. Available at (22.04.2018): <https://antibiotic.ecdc.europa.eu/en/communication-toolkit-professionals-hospitals-and-other-healthcare-settings>
- ¹⁷ WHO (World Health Organisation) Evidence of hand hygiene to reduce transmission and infections by multidrug resistant organisms in healthcare settings. Geneva: WHO; 2014. Available at (22.04.2018): http://www.who.int/gpsc/5may/MDRO_literature-review.pdf
- ¹⁸ ECDC (European Centre for Disease Prevention and Control), EFSA (European Food Safety Authority), and EMA (European Medicines Agency), 2017. ECDC/EFSA/EMA second joint report on the integrated analysis of the consumption of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from humans and food-producing animals – Joint Interagency Antimicrobial Consumption and Resistance Analysis (JIACRA) Report. *EFSA Journal* 2017;15(7):4872,135. doi:10.2903/j.efsa.2017.4872. Available at (25.02.2018): <https://www.efsa.europa.eu/en/efsajournal/pub/4872>
- ¹⁹ Guidelines for the prudent use of antimicrobials in veterinary medicine (2015/C 299/04). Available at (12.04.2018): [http://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1523547946385&uri=CELEX:52015XC0911\(01\)](http://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1523547946385&uri=CELEX:52015XC0911(01))
- ²⁰ ECDC (European Centre for Disease Prevention and Control), Surveillance of antimicrobial resistance in Europe, Annual report of the European Antimicrobial Resistance Surveillance Network (EARS-Net), 2016. Available at (22.04.2018) <https://www.ecdc.europa.eu/sites/portal/files/documents/AMR-surveillance-Europe-2016.pdf>
- ²¹ Antibacterial agents in clinical development: an analysis of the antibacterial clinical development pipeline, including tuberculosis. Geneva: World Health Organization; 2017 (WHO/EMP/IAU/2017.12). Licence: CC BY-NC-SA 3.0 IGO. Available at (25.02.2018): <http://apps.who.int/iris/bitstream/10665/258965/1/WHO-EMP-IAU-2017.11-eng.pdf?ua=1>
- ²² Dar, Osman A et al. Exploring the evidence base for national and regional policy interventions to combat resistance. *The Lancet*, Volume 387, Issue 10015, 285 - 295.
- ²³ C. Pulcin et al. Ensuring universal access to old antibiotics: a critical but neglected priority, *Clinical Microbiology and Infection* 23 (2017) 590-592.