

Antimicrobial resistance related to food production: International cooperation and EU action

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1.- Antimicrobial resistance, a growing global concern

1.1. The threat of antimicrobial resistance

The discovery of antimicrobials in the twentieth century is undoubtedly one of the most significant accomplishments in human clinical medicine. The term refers to substances used to kill microorganisms or to inhibit their growth and multiplication and includes antibiotics, which are specifically employed against bacteria. Initially introduced in the 1930s, antimicrobial agents have revolutionized the entire medical practice and our way of living, enabling the successful treatment of numerous infections, which were considered lethal even in the context of simple surgical procedures. Today, antimicrobial substances are not only essential for curing infectious diseases but are also deemed vital for reducing the risk of complications in relation to various significant medical operations, such as cancer chemotherapy, organ transplants and the care of premature babies¹.

However, soon after the introduction and first uses of penicillin, the issue of antimicrobial resistance (AMR) emerged and has become now one of the most critical public health challenges. AMR is defi-

ned by the World Health Organization (WHO) as “*resistance of a microorganism to an antimicrobial drug that was originally effective for treatment of infections caused by it*”². More specifically, antimicrobial resistance refers to the ability of microorganisms – bacteria, viruses, parasites, and fungi – to tolerate and withstand affordable and effective first choice antimicrobial cures, threatening the effective prevention and treatment of an ever-expanding range of infections.

AMR is a natural phenomenon, which occurs over time through genetic changes and microbial adaptation to the environment. Nevertheless, it has been exacerbated by both an abuse and misuse of antimicrobials.

Several factors have caused such inappropriate and excessive consumption, including a use for non-therapeutic purposes, over-the-counter and internet sales, the pollution of the environment by antimicrobials and, predominantly, a general lack of regulation and professional oversight, both nationally and internationally³.

The consequences of this phenomenon are self-evidently severe, such as treatment failures and consequent more lasting and serious diseases, increased hospitalization rates, growing mortality, productivity losses and reduced livelihoods⁴. A 2011 WHO Report estimates that 25 000 people die annually in the European Union from infections caused by antibiotic-resistant bacteria⁵. A more recent study conducted by the Food and Agriculture Organization (FAO) predicts even more alarming numbers: the effects of AMR are assessed at 10 million human fatalities annually and a 2 to 3.5 percent decrease in global Gross Domestic Product, or USD 100 trillion, by 2050⁶.

Medicine is approaching a situation similar to the pre-antibiotic era and antimicrobial resistance is emerging as a looming public health crisis.

(¹) European Commission, *Communication from the Commission to the European Parliament and the Council. Action plan against the rising threats from Antimicrobial Resistance*, November 2011, p. 2.

(²) World Health Organization, *Antimicrobial resistance. Fact sheet n.194*, April 2014, p.1.

(³) Food and Agriculture Organization of the United Nations, *The FAO Action Plan on antimicrobial resistance. 2016-2020*, 2016, p. 1.

(⁴) Ibidem.

(⁵) World Health Organization, Regional Office for Europe, *Tackling antibiotic resistance from a food safety perspective in Europe*, 2011, p. xiii.

(⁶) *The FAO Action Plan on antimicrobial resistance. 2016-2020*, cit., p. 1.

1.2.- Antimicrobial resistance in relation to food production

Since their introduction, antimicrobials have not only been applied in human medicine but also as veterinary drugs to treat animal diseases and in agriculture to prevent and control infections and to improve feed efficiency⁷. Over the past fifty years, population growth and economic expansion have determined a significant intensification in the demand for food, thus causing an increase in global food production, and, in parallel, a growth in the use of antimicrobials in agriculture⁸.

While it is difficult to evaluate the exact quantity of antimicrobials used in food production, because of poor surveillance and data collection in many countries, evidence suggests that such amount is at least comparable to the quantity used for humans. Certain countries show a far greater consumption in agriculture than in human medicine: the United States, for instance, use 70 percent of the total amount of antibiotics for veterinary purposes and consumption of antimicrobials in meat production in Brazil, Russia, India, China and South Africa is set to double by 2030⁹. Global consumption of antimicrobials in food animal production by 2030 is expected to rise by two-thirds¹⁰. Concern is also raised in relation to an increasing use of antifungals in crop culture¹¹.

It is undeniable that antimicrobial drugs are an essential tool to preserve animal life and welfare, safe trade, efficient production and food security. However, it is also crucial that some of these sub-

stances are limited to protecting human health and to fighting infections in humans exclusively¹². Additionally, much of the use of antimicrobials in animals is not for therapeutic purposes: in fact, relevant amounts of these medicines are used as a prophylactic amongst healthy animals to prevent the spread of a disease within a herd or flock or as growth promoters¹³, to enhance animal weight.

Abuse and misuse of antimicrobial medicines in food animals, and in agriculture more generally, holds severe consequences for public health, as it promotes the development of resistant microorganisms, which can then be passed on to humans¹⁴. The transfer may happen through various routes. Drug resistant organisms may pass on through direct contact between animals and humans – notably people engaged in husbandry. More generally, interaction may occur along the food chain and processing steps— particularly during slaughtering, transportation, storage and while consumers prepare or eat the meat itself. Furthermore, threat to human health may result from animal excretion and waste of both resistant microorganisms and drugs into the environment, including water¹⁵, which can then serve as the reservoir of antibiotic-resistance genes¹⁶. Manure from farm animals is often used as fertilizer on crop cultures, thus fruits and vegetables may be contaminated as well and constitute an additional transmission path to food consumers.

1.3.- The need for an international cooperation

AMR is a major health concern and a food safety

(⁷) V. Economou, P. Gousia, *Agriculture and food animals as a source of antimicrobial-resistant bacteria*, in *Dove Medical Press*, April 2015, pp.49-61.

(⁸) Food and Agriculture Organization of the United Nations, *Antimicrobial Resistance and our food systems: challenges and solutions*, 2016, p. 2.

(⁹) J. O'Neill, *Antimicrobials in agriculture and the environment: reducing unnecessary use and waste*, Review on Antimicrobial Resistance, December 2015, p. 1.

(¹⁰) A. D. So et al., *International Agreement to Address the Contribution of Animal Agriculture to Antibiotic Resistance: A One Health Approach*, in *Journal of Law, Medicine and Ethics*, summer 2015, p. 38.

(¹¹) J. O'Neill, *Tackling drug-resistant infections globally: final report and recommendations*, Review on Antimicrobial Resistance, April 2016, p. 24.

(¹²) *Antimicrobial Resistance and our food systems: challenges and solutions*, cit., p. 3.

(¹³) While the European Union has withdrawn antimicrobial growth promoters (AGPs) in 2006, numerous other countries still use AGPs, including the United States. See *Agriculture and food animals as a source of antimicrobial-resistant bacteria*, cit.

(¹⁴) *Tackling antibiotic resistance from a food safety perspective in Europe*, cit., p. xiii.

(¹⁵) *Antimicrobials in agriculture and the environment: reducing unnecessary use and waste*, cit., p. 1.

(¹⁶) *Agriculture and food animals as a source of antimicrobial-resistant bacteria*, cit.

challenge. As food animals and food products are traded worldwide, as people travel globally, such phenomenon does not abide by any national border. Resistant microorganisms arising in humans, animals or the environment may spread from one to the other and from country to the other¹⁷.

AMR represents a global and multifactorial issue. Curbing the emergence of resistant organisms not only requires a “One Health” approach, which underlines the importance of a multi-sectoral coordination on the safety of humans, animals and the environment¹⁸. It also emphasizes the need for global concerted actions by public and private organizations, at national and international level.

AMR has been acknowledged by several international organizations as part of a global commitment to deal with the issue in a concerted manner.

2.- The OIE-WHO-FAO cooperation

2.1.- The Tripartite Alliance.

The three supranational entities most involved in tackling AMR are indisputably the World Health Organization (WHO), the Food and Agriculture Organization (FAO) – both specialized agencies of the United Nations - and the World Organisation for Animal Health (OIE), a 1924-born intergovernmental organization with 180 member countries.

Recognizing that the rising threat of antimicrobial resistant agents requires a holistic and multi-institutional approach, WHO, FAO and OIE have been engaged, since 2010, in a Tripartite Partnership that lays down respective responsibilities to address health risks at the human-animal-ecosystems inter-

faces. In the fight against AMR, their goals are to ensure that antimicrobial agents maintain their efficacy, promote prudent and responsible use of these agents and facilitate global access to quality drugs¹⁹. Tripartite meetings are held annually to improve coordination.

Under the framework of the Tripartite Alliance, the three organizations have developed governance structures, early warning systems and supporting mechanisms to member countries, in the spirit of a strong multi-sectoral collaboration²⁰. WHO and FAO participate in OIE's relevant working groups' meetings, including the OIE Working Group on Animal Production Food Safety (APFS), which was created to adopt guidelines on the responsibility of veterinary services in improving food safety. Moreover, the three organizations have established the Global Early Warning System for Major Animal Diseases, including Zoonoses (GLEWS), a joint system that combines alert and response mechanisms, improves data sharing and risk assessment and assists in early warning, prevention and control of animal disease threats. GLEWS is linked with the International Food Safety Authorities Network (INFOSAN), developed jointly by FAO and WHO to alert national focal points on the occurrence of regional or global events related to food safety²¹. Regionally, FAO and OIE have created the Regional Animal Health Centres (RAHCs) to provide technical support to member countries concerning national and local projects and their adherence to international standards. RAHCs work in the context of the Global Framework for the Control of Transboundary Animal Diseases, launched in 2004 by OIE and FAO to provide a response framework to endemic and emerging infectious diseases²². And

(17) Food and Agriculture Organization of the United Nations, World Organisation for Animal Health and World Health Organization, *WHO, FAO, and OIE unite in the fight against Antimicrobial Resistance*, p.1.

(18) Ibidem.

(19) World Organisation for Animal Health, *Antimicrobial resistance. Summary of OIE activities*, July 2015, p. 9; see also WHO website on FAO/OIE/WHO Tripartite Collaboration on AMR.

(20) Food and Agriculture Organization of the United Nations, World Organisation for Animal Health and World Health Organization, *The FAO-OIE-WHO Collaboration. Sharing responsibilities and coordinating global activities to address health risks at the animal-human-ecosystems interfaces. A Tripartite Concept Note*, April 2010, p. 3.

(21) J. O'Neill, *Tackling drug-resistant infections globally: final report and recommendations*, Review on Antimicrobial Resistance, April 2016, p. 24.

(22) *The FAO-OIE-WHO Collaboration. Sharing responsibilities and coordinating global activities to address health risks at the animal-human-ecosystems interfaces. A Tripartite Concept Note*, cit., pp. 3-4.

the three organizations have committed to work more closely together to address new social demands for safe food and animal welfare²³.

2.2.- *The Global Action Plan on Antimicrobial Resistance*

At the Sixty-eighth World Health Assembly in May 2015, the Assembly adopted a Global Action Plan (GAP)²⁴ to ensure continuity of successful antimicrobial treatment and prevention of infectious diseases, through the use of good-quality and worldwide accessible medicines. To reach this goal, the GAP sets out five strategic objectives. First, action is required in order to improve awareness and understanding of antimicrobial resistance through effective and audience-targeted communication, education and training. Secondly, gaps need to be filled in relation to surveillance and research to strengthen our knowledge of AMR on all aspects (i.e. incidence, geographical patterns and spreading times). Third, it is necessary to reduce the incidence of infections through effective sanitation, hygiene and prevention measures. Fourth, initiatives need to be taken to optimize the use of antimicrobial medicines in human and animal health and to regulate their distribution and quality. Finally, there is an essential need to develop the economic case for sustainable investment that takes into account all countries and to increase investment in new medicines, diagnostic tools, vaccines and other interventions²⁵.

The Plan has received endorsement from both FAO and OIE. More specifically, FAO's Thirty-ninth Conference adopted Resolution 4/2015 in June 2015, which recognizes the serious threat of AMR to a sustainable food production and the need for an effective response that involves all public and priva-

te sectors. The subsequent FAO Action Plan on Antimicrobial Resistance²⁶, in support of the WHO-led Global Action Plan, highlights the importance of a "One Health" approach and responds to the GAP call to action in implementing AMR measures in the food and agriculture sectors²⁷. The GAP emphasizes also the role of the OIE in the fight against AMR in animals and OIE World Assembly of Delegates, held in May 2015, has pledged its support to the Plan through Resolution n.26²⁸.

The GAP lays down the framework for national action plans (NAPs). All Member States are required to set up, within two years of the endorsement of the plan by the Health Assembly, programmes on antimicrobial resistance in line with the Global Action Plan and FAO, OIE and Codex Alimentarius standards. These national plans must assess the resources needed to tackle AMR in each country and a manual to help governments in the development of such plans has been created jointly by the three organizations²⁹.

That WHO, OIE and FAO took the step of closely working together on the challenge of rising drug resistance, with the participation of all their Member Countries, is testament to the urgency and high stakes at play³⁰.

2.3.- *Codex Alimentarius.*

International cooperation in the fight against resistance is further carried out through the Codex Alimentarius Commission (CAC), created in 1963 by FAO and WHO under their Joint Food Standards Programme. The Programme was set to promote coordination of all food safety initiatives undertaken by international organizations and the subsequent Commission was established as a joint intergovern-

⁽²³⁾ Ibidem, p. 5.

⁽²⁴⁾ World Health Organization, *Global action plan on antimicrobial resistance*, 2015.

⁽²⁵⁾ Ibidem, p. vii.

⁽²⁶⁾ *The FAO Action Plan on antimicrobial resistance. 2016-2020*, cit.

⁽²⁷⁾ Ibidem, p. vi.

⁽²⁸⁾ *Antimicrobial resistance. Summary of OIE activities*, p. 9. See also Resolution n.26, *Combating Antimicrobial Resistance and Promoting the Prudent Use of Antimicrobial Agents in Animals*.

⁽²⁹⁾ Food and Agriculture Organization of the United Nations, World Organisation for Animal Health and World Health Organization, *Antimicrobial resistance. A manual for developing national action plans*, February 2016.

⁽³⁰⁾ *Antimicrobials in agriculture and the environment: reducing unnecessary use and waste*, cit., p. 28.

mental body, to specifically guarantee consumers' health and ensure fair practices in the commerce of food³¹. OIE contributes to the Commission's work on food, animal and health aspects³².

Several CAC's subsidiary bodies focus on the various implications of using antimicrobials in food animals, including the Committee on Residues of Veterinary Drugs in Foods, the Committee on Food Hygiene and the ad hoc Intergovernmental Task Force on Animal Feeding, each dealing with the phenomenon within their respective discipline. In 2006, the Commission created an ad hoc Intergovernmental Task Force on Antimicrobial Resistance, acknowledging the urgency for a more specific attention to the matter³³.

WHO and FAO work collaboratively through the Codex to adopt international food safety standards for nontoxic medicines residue levels and feeding practices and to set microbiological risk profiles³⁴. Specific Codex texts related to AMR are the Code of Practice to Minimize and Contain Antimicrobial Resistance³⁵ and the Guidelines for Risk Analysis of Foodborne Antimicrobial Resistance³⁶.

The 2005 Code of Practice seeks to minimize the health threats of antimicrobials' consumption in food animals by calling for veterinary oversight and stressing the importance of alternatives to antimicrobials³⁷.

The document lays down the principle according to which *"the responsible use of veterinary antimicrobial drugs in food-producing animals [...] does not include the use for growth promotion of veterinary antimicrobial drugs that belong to or are able to cause cross resistance to classes of antimicrobial agents used [...] in humans in the absence of a risk analysis"*.

The Code defines the responsibilities of various stakeholders engaged in the authorization, manufacture, distribution and consumption of veterinary antimicrobials to protect consumer's health, to maintain animal health and to prevent antimicrobials' contamination of food.

Identifying risk analysis as an essential tool to evaluate threats to human health deriving from AMR, and in particular food related resistant agents, the 2011 Guidelines provide a guiding framework concerning science-based methods for risk analysis of foodborne AMR. With the goal of determining the most appropriate risk management strategies, such analysis is intended to assist in evaluating risks of resistance in microorganisms, risks of presence of resistant agents in food and animal feed and risks of transmission to humans through various foodborne routes.

Since the creation of the World Trade Organization (WTO) in 1995, the relevance of Codex standards – and that of OIE guidelines, as well – has significantly increased. In fact, WTO recognizes CAC and OIE texts as the benchmarks for food safety and animal health and encourages its Members, through its Agreement on the Application of Sanitary and Phytosanitary Measures³⁸, to adopt national measures in accordance with such texts³⁹.

3.- European Union action at international level

3.1.- EU legal framework on foodborne AMR

The European Union (EU) has been active for more than fifteen years in the fight against the ever-presing concern of AMR, in the light of the overarching protection of human health, based on art.168

⁽³²⁾ The FAO-OIE-WHO Collaboration. *Sharing responsibilities and coordinating global activities to address health risks at the animal-human-ecosystems interfaces. A Tripartite Concept Note*, cit., p. 3.

⁽³³⁾ *Tackling antibiotic resistance from a food safety perspective in Europe*, cit., p. 53.

⁽³⁴⁾ A. D. So et al., *International Agreement to Address the Contribution of Animal Agriculture to Antibiotic Resistance: A One Health Approach*, cit., p. 40.

⁽³⁵⁾ The CAC/RCP 61-2005 text may be found at: Food and Agriculture Organization of the United Nations, World Health Organization, *Codex texts on foodborne antimicrobial resistance*, pp. 49 et seq.

⁽³⁶⁾ The CAC/GL 77-2011 text may be found at: *Codex texts on foodborne antimicrobial resistance*, cit., pp. 8 et seq.

⁽³⁷⁾ D. F. Maron et al., *Restrictions on antimicrobial use in food animal production: an international regulatory and economic survey*, in *BioMed Central*, October 2013.

⁽³⁸⁾ World Trade Organization, *Agreement on the application of sanitary and phytosanitary measures*, 1995.

⁽³⁹⁾ *Tackling antibiotic resistance from a food safety perspective in Europe*, cit., p. 61.

TFEU⁴⁰. Over the years, multiple regional initiatives have been endorsed, comprising measures specifically pertinent to foodborne resistance and antibiotics' use in food animals. Regulation (EC) 1831/2003 on additives for use in animal nutrition⁴¹ is undoubtedly one of the most relevant EU laws on AMR as it bans the use of antibiotics growth promoters (AGPs) as of January 2006. Mandatory monitoring of AMR in zoonotic and commensal bacteria from animals is carried out under Directive 2003/99/EC⁴² and the vigilance and reporting priorities from the public health point of view are laid out in Commission Implementing Decision 2013/652/EU⁴³. The latter entered into force in 2014, as did Commission Implementing Decision 2013/653/EU⁴⁴, which concerns financial aid towards a coordinated control plan for AMR monitoring in zoonotic agents. Directive 2001/82/EC on the Community code relating to veterinary medicinal products⁴⁵ provides that maximum residue limits (MRLs) must be established before any substance may be used in a veterinary medical product intended for food animals. Such provision takes into account potential adverse effects on public health due to residues of the substance, including antimicrobials, in food products derived from treated animals.

As for more recent initiatives, the European Parliament and the Council adopted in 2016 a new Animal Health Law through Regulation (EU) 2016/429⁴⁶ on transmissible animal diseases. The Regulation is part of a package of measures proposed by the Commission in May 2013 to strengthen the enforcement of health and safety standards for the whole agri-food chain. In relation to AMR, the

new Law establishes the first ever link between animal welfare and public health in EU law, and sets out a better legal basis for monitoring resistant animal pathogens, thus contributing to a health status based on prevention rather than cure. Moreover, in September 2015 the European Commission published the Guidelines for the prudent use of antimicrobials in veterinary medicine (2015/C 299/04)⁴⁷, which are addressed to Member States, industry partners, farmers, veterinarians and associations. Their purpose is to provide practical guidance on the development and implementation of strategies to promote the prudent use of antimicrobials in veterinary medicine. Finally, it is worth mentioning that a Regulation⁴⁸ has been proposed in 2014 on the manufacture, placing on the market and use of medicated feed, in order to repeal the outdated Directive 90/167/EEC. The proposal lays down specific rules for the prescription and use of medicated feed containing antimicrobials in food-producing animals.

In addition to the regional initiatives within the Union⁴⁹, EU international action has been endorsed by the Action Plan against the Rising Threats from Antimicrobial Resistance⁵⁰, adopted by the European Commission in 2011. The Plan, indeed, identifies international cooperation with supranational partners as one of the seven key areas where measures against resistance are most urgently needed⁵¹.

3.2.- Multilateral Cooperation.

The European Commission actively supports

⁽⁴⁰⁾ The Treaty on the Functioning of the European Union may be found here.

⁽⁴¹⁾ The Regulation may be found here.

⁽⁴²⁾ The Directive may be found here.

⁽⁴³⁾ The Decision may be found here.

⁽⁴⁴⁾ The Decision may be found here.

⁽⁴⁵⁾ The Guidelines may be found here.

⁽⁴⁶⁾ The Regulation may be found here.

⁽⁴⁷⁾ The Directive may be found here.

⁽⁴⁸⁾ The Proposal may be found here.

⁽⁴⁹⁾ For a comprehensive overview of EU's actions, legislations, surveillance programmes and research initiatives, see European Commission's website on Action at EU Level.

⁽⁵⁰⁾ European Commission, Directorate-General for Health and Consumers, *Communication from the Commission to the European Parliament and the Council. Action plan against the rising threats from Antimicrobial Resistance*, COM (2011) 748, November 2011.

⁽⁵¹⁾ Action at EU Level, cit.

WHO's mandate in the context of its Global Action Plan against AMR and collaboration is mostly engaged with WHO-Europe, based on the Health Security Roadmap⁵². The cooperation includes implementation of the WHO European Strategic Action Plan on Antibiotic Resistance⁵³, the Council Recommendation on the Prudent Use of Antimicrobial Agents in Human Medicine⁵⁴ and particularly the Action Plan against the Rising Threats from Antimicrobial Resistance. The Commission also funds the European Reference Laboratory for Antimicrobial Resistance (EURL-AMR), which supports the initiatives of both the WHO Global Foodborne Infections Network (GFN) and the WHO Advisory Group in Surveillance of Antimicrobial Resistance (AGISAR) with the aim to develop global standards for the monitoring of AMR. The Laboratory similarly cooperates with Member countries in relation to capacity building for AMR surveillance in the food production and consumption chain⁵⁵.

In the veterinary sector, the European Union has been contributing to OIE's fight against AMR. Technical specialists of the Commission, the European Medicines Agency (EMA) and the European Food Safety Authority (EFSA) have participated in the development of the OIE Standards on Antimicrobial Resistance⁵⁶ and in the revision of the AMR related chapters of the OIE Terrestrial Animal Health Code. Additionally, EU experts contribute to the creation of the OIE-led global database on the use of antimicrobial agents in animals⁵⁷.

EU international cooperation is further undertaken through the Codex Alimentarius. European experts actively contributed to the drafting of the Guidelines

for Risk Analysis of Foodborne Antimicrobial Resistance. The Guidelines' processes and methodologies are followed by the European Commission and its agencies, and constitute the foundation of their risk assessment activities to evaluate the risk to human health associated to foodborne AMR⁵⁸.

3.3.- Bilateral cooperation.

EU international collaboration against AMR has also started on a bilateral basis. The Transatlantic Taskforce on Antimicrobial Resistance (TATFAR)⁵⁹ was established in 2009 with the goal of improving cooperation between the United States and the EU in three key areas: 1) appropriate therapeutic use of antimicrobial drugs in medical and veterinary communities; 2) prevention of drug resistant infections and 3) strategies for improving the pipeline of new antimicrobial drugs. TATFAR has led to effective information exchange, understanding of best practices and has been extended to include Canada and Norway⁶⁰. In relation to foodborne AMR, the Taskforce has particularly been working on creating an international working group to identify key knowledge gaps in understanding the transmission to man arising from animals' consumption of antimicrobials⁶¹.

In recent years, the issue of AMR has similarly represented the topic of dialogue in the context of EU bilateral collaboration with China and the Russian Federation and the European Commission services are currently contributing to the work against antimicrobial resistance in several developing countries⁶².

⁽⁵²⁾ European Commission, *Commission staff working document. Progress report on the Action plan against the rising threats from Antimicrobial Resistance*, March 2015, p. 14.

⁽⁵³⁾ World Health Organization, Regional Office for Europe, *European strategic action plan on antibiotic resistance*, June 2011.

⁽⁵⁴⁾ Council of the European Union, *Recommendation of 15 November 2001 on the prudent use of antimicrobial agents in human medicine*, November 2001.

⁽⁵⁵⁾ European Commission, *Antimicrobial resistance (AMR). Evaluation of the 2011-2016 action plan*, 2016, p. 3.

⁽⁵⁶⁾ World Organisation for Animal Health, *International Standards on Antimicrobial Resistance*, 2003.

⁽⁵⁷⁾ Commission staff working document. *Progress report on the Action plan against the rising threats from Antimicrobial Resistance*, cit., p. 15.

⁽⁵⁸⁾ Ibidem, p. 15.

⁽⁵⁹⁾ TATFAR website: <https://www.cdc.gov/drugresistance/tatfar/>.

⁽⁶⁰⁾ *Antimicrobial resistance (AMR). Evaluation of the 2011-2016 action plan*, cit., p. 3.

⁽⁶¹⁾ Commission staff working document. *Progress report on the Action plan against the rising threats from Antimicrobial Resistance*, cit., p. 15.

⁽⁶²⁾ Ibidem, p. 15.

4.- *Increasing international attention*

The ever-growing concern over resistant microorganisms is testified by two very recent initiatives at international level.

4.1.- *WHO-WTO-WIPO Joint Technical Symposium on AMR*

On October 2016, the World Trade Organization, the World Intellectual Property Organization (WIPO) and the World Health Organization convened a Joint Technical Symposium on AMR, to discuss the challenges of resistance and potential ways forward for strategic collaboration⁶³. The Symposium stressed the urgency of global actions across countries and WHO specified how antimicrobial resistance has been undergoing a major transition: it is no longer regarded as a complex technical issue for a limited audience but as a vital threat for humanity, similar to climate change⁶⁴.

The Symposium focused on current initiatives and challenges of research and development on AMR and analysed the potential role of trade policy in support of antimicrobial access and stewardship. On this latter subject, WTO Director-General Roberto Azevêdo highlighted how several WTO instruments – including the Trade Facilitation Agreement, the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), the Agreement on Sanitary and Phytosanitary Measures (SPS) and the Technical Barriers to Trade (TBT) Agreement – provide a legal framework that encourages the responsible use of antibiotics and allows members to take necessary measures to protect human health or the environment. Even if

these restrict the trade of certain products⁶⁵.

4.2.- *United Nations Interagency Coordination Group on Antimicrobial Resistance*

On October 2016, during the 71st Session of the United Nations General Assembly, Member States recognized the scale of AMR and adopted the Political Declaration of the High-level Meeting on Antimicrobial Resistance⁶⁶ (contained in Resolution A/RES/71/3).

Its Paragraph 15 requests the Secretary-General to establish, in consultation with FAO, OIE and WHO, an ad hoc inter-agency coordination group, to provide guidance to sustained effective global action against AMR. Such Group has been officially established on the last 17th of March: co-chaired by the UN Deputy Secretary-General and the WHO Director General, it will be comprised of high-level representatives of relevant UN agencies, other international organizations, and individual experts across different sectors, including animal health, agriculture, and environment⁶⁷.

5.- *The way forward*

Notwithstanding the multiple international initiatives against AMR, the gaps are still severe. Specifically, there remains a significant need for scientific information on the various aspects of resistance, in order to have a full understanding of the scope of such phenomenon. Data are currently provided on a voluntary basis, and the methods used to collect evidence are not standardized or fully transparent. Several reports⁶⁸ call for harmonized efforts and effective investments to expand on the corpus of

⁽⁶³⁾ WHO website on *Antimicrobial Resistance: How to Foster Innovation, Access and Appropriate Use of Antibiotics? A Joint Technical Symposium by WHO, WIPO and WTO*.

⁽⁶⁴⁾ WTO website on *Symposium underlines need for global cooperation in addressing antimicrobial resistance*.

⁽⁶⁵⁾ Ibidem.

⁽⁶⁶⁾ Resolution adopted by the General Assembly on 5 October 2016, A/RES/71/3, *Political declaration of the high-level meeting of the General Assembly on antimicrobial resistance*.

⁽⁶⁷⁾ United Nations website on *Interagency Coordination Group on Antimicrobial Resistance*.

⁽⁶⁸⁾ T. F. Landers et al., *A Review of Antibiotic Use in Food Animals: Perspective, Policy, and Potential*, in *Public Health Reports*, January 2012; A. D. SO et al., *International Agreement to Address the Contribution of Animal Agriculture to Antibiotic Resistance: A One Health Approach*, cit., p.41; European Commission, *Antimicrobial resistance (AMR). Evaluation of the 2011-2016 action plan*, cit., p. 1; *Communication from the Commission to the European Parliament and the Council. Action plan against the rising threats from Antimicrobial Resistance*, cit., pp. 11 ss; a contrario, F. M. Aarestrup, *The livestock reservoir for antimicrobial resistance: a*

knowledge, which requires, in parallel, effective surveillance of antimicrobials' production and administration to food animals.

Such focus on the need of more serious data collection and monitoring mechanisms, significant research on alternatives to antimicrobial drugs, harmonized global standards in sampling methodology, diagnostic protocols and reporting procedures testifies that the fight against AMR is, for many aspects, still at the research, discussion and study stage. Moreover, major international instruments on resistance take the form of standards, guidelines and plans. The recent WHO-WTO-WIPO Symposium and the newly established UN Interagency Coordination Group confirm that international action is far from effective (let alone binding) measures.

As AMR is on a ticking clock, an international agreement might be required to accelerate the fight against resistance, by providing a comprehensive and harmonized framework on monitoring, implementation, reporting of progress, and financing of the required activities. An initial international agreement among targeted parties, rather than a universally inclusive arrangement, might also be conside-

red. And existing texts and initiatives would understandably constitute a precious foundation of the project.

ABSTRACT

The discovery of antimicrobials is unquestionably one of the major medical breakthroughs of the twentieth century, not only in relation to human health but also in connection with animal husbandry and food production. Unfortunately, from the very first use of antimicrobial agents, the resistance clock has started ticking and AMR is now emerging as one of the most urgent public health concerns, requiring a high-level attention at international level. The article analyses the various concerted initiatives undertaken by international organizations and the European Union, revealing where global cooperation in the fight against AMR currently stands and calling for an urgent acceleration of international action through more effective – and possibly binding – measures.

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