The Role of the European Food Safety Authority (EFSA) in the Fight against Antimicrobial Resistance (AMR)

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SUMMARY

The European Food Safety Authority (EFSA) is an agency funded by the European Union that acts as a source of scientific advice and communication on risks associated with the food chain. EFSA is actively involved in many activities in the area of antimicrobial resistance (AMR). It provides scientific advice used to support the European legislator and Member States in making effective and timely risk management decisions in the fight against AMR for example, in reducing the need to use antimicrobials in food-producing animals or in managing emerging threats such as resistance of microorganisms to beta-lactams, carbapenems and colistin. EFSA provides advice on how to monitor AMR in food-producing animals and food, and gathers and analyzes data collected at the national level in Europe. Finally, it actively communicates the risks linked to antimicrobial resistance. This paper provides an overview of the activities of EFSA in the area of AMR.

OVERVIEW

The European Food Safety Authority (EFSA) was set up in January 2002, following a series of food crises in the late 1990s (bovine spongiform encephalopathy, dioxin contamination, foot and mouth disease, etc.), as part of a comprehensive program to improve European Union (EU) food safety systems, to ensure a high level of consumer protection and to restore and maintain trust in the EU food supply. As risk assessor, EFSA produces scientific opinions and advice to provide a sound foundation for European policies and legislation in the food and feed safety sector and to support the European Commission, European Parliament and EU Member States in taking effective and timely risk management decisions. EFSA is also responsible for related risk communication.

Combating antimicrobial resistance (AMR) is a priority for the EU and its Member States. The EU has developed a series of EU-wide policy and legislative initiatives for the control or prevention of AMR in the field of human medicine, in the veterinary and food safety area and in relation to monitoring, research, prevention and international cooperation. AMR is among the topics of competence of EFSA. Antimicrobials are commonly used in human and veterinary medicine to treat a wide variety of infectious diseases. The use of antimicrobials in both humans and animals, especially when overused or misused, inevitably exerts selection pressure towards antimicrobial-resistant bacteria and has been linked to the emergence and spread of AMR, rendering treatments ineffective and ultimately posing a serious risk to both public health and animal health. In 2009, the European Centre for Disease Prevention and Control (ECDC) and the European Medicines Agency (EMA) estimated that each year about 25,000 patients die in the EU from an infection caused by multidrug-resistant bacteria *(7)*. The European Commission published on 2011 its first Action Plan against the rising threats from AMR *(1)*, identifying seven areas of priority for action against AMR, and launched, in 2017, its second AMR Action Plan *(4)*. EFSA is one of the key players identified in the Action Plan and is actively involved in many activities in the area of AMR, from the monitoring of AMR in bacteria from food-producing animals and food to the provision of scientific advice and risk assessment, often in close collaboration with other EU agencies, such as ECDC and EMA. The aim of this paper is to provide an overview of the activities of EFSA in the area of AMR, the latest activities carried out and the ones in the pipeline.

MONITORING OF ANTIMICROBIAL RESISTANCE

AMR monitoring in food-producing animals and food

Antimicrobial resistant bacteria can spread to humans through many different routes. These include transmission from animals to humans through direct contact, but also through food or other routes such as water or environmental contamination with antimicrobial-resistant bacteria of animal origin. Some zoonotic bacteria can be resistant to antimicrobials and potentially lead to infections in humans. *Campylobacter* spp., *Salmonella* spp., some strains of *Escherichia coli*, and occasionally methicillin-resistant *Staphylococcus aureus* (MRSA) are examples of zoonotic bacteria that can infect people by the foodborne route. Other commensal bacteria that can live both in animals and humans, such as *E. coli* and *Enterococcus* spp., can also carry AMR genes that can be transferred between bacterial species, including organisms capable of causing disease in both humans and animals. Therefore, monitoring of AMR in zoonotic and commensal bacteria in food-producing animals and food thereof is useful for assessing the occurrence and better understanding the distribution and evolution of antimicrobial-resistant bacteria as well as the contribution of those sources to AMR in humans. It also provides relevant risk assessment data and the opportunity to evaluate the effect of targeted interventions, in particular when combined with data on antimicrobial consumption (AMC). It also allows identification of emerging patterns of resistance in food-producing animals and food.

At the EU level, EFSA is responsible for collecting and analyzing data on AMR gathered by the EU Member States on the occurrence of antimicrobial-resistant bacteria in food-producing animals and derived food. It is assisted by EFSA's network on zoonoses data collection, a pan-European network of national representatives of EU Member States, European Free Trade Association (EFTA) countries, and EU candidate and potential candidate countries. On a yearly basis, EFSA produces, in close collaboration with ECDC, the EU Summary Report on AMR (EUSR-AMR), which includes data on the occurrence of AMR and multidrug resistance (MDR) in zoonotic and indicator bacteria from food-producing animals and food, as well as in *Salmonella* spp. and *Campylobacter* spp. isolates from human cases of foodborne infections. The first EUSR-AMR report covered years 2004–2007 *(15)*, while the last one available covers human and animal/food data in 2015 *(6)*.

EFSA also published baseline survey reports on the prevalence of antimicrobial-resistant bacteria in the EU in specific animal populations, such as MRSA in breeding pigs *(12, 14)*, and has regularly provided guidance to national authorities on how to carry out AMR monitoring and reporting activities *(16, 17, 18, 19, 21)*. Scientific advice from EFSA *(17, 18)* was the basis of the reviewed legislation on harmonized monitoring of AMR in food-producing animals and food thereof (Commission Implementing Decision 2013/652/EU). The new legislation established a list of combinations of bacterial species, panels of antimicrobial substances, food-producing animal populations and food products subject to AMR monitoring by EU Member States. Following the publication of the new legislation on AMR monitoring, EFSA developed detailed technical specifications on randomized sampling for harmonized monitoring of AMR in zoonotic and commensal bacteria *(19)*, to give guidance to Member States and ensure that representative sampling is carried out. The new legislation set up priorities for the monitoring of AMR from a public health perspective, while improving the comparability and reliability of the AMR data collected.

Following the implementation of the Decision as of January 2014, monitoring of AMR in *E. coli* became mandatory, as it is for *Salmonella* spp. and *Campylobacter jejuni* in the major food-producing animal populations and meat thereof, with a biennial schedule (broilers, laying hens and fattening turkeys on even years, and fattening pigs and bovines under one year of age on uneven years). Specific monitoring of extended-spectrum beta-lactamase (ESBL), AmpC beta-lactamase (AmpC) and carbapenemase-producing *Salmonella* spp. and indicator commensal *E. coli* was also introduced. Data on the prevalence, genetic diversity and resistance of MRSA are provided to EFSA on a voluntary basis. The collection and reporting of data are to be performed at the isolate level, to allow more in-depth analyses to be conducted, in particular on the occurrence of MDR. Microdilution methods for testing shall be used and results should be interpreted by the application of the European Committee on Antimicrobial Susceptibility testing (EUCAST) epidemiological cut-off (ECOFF) values for the interpretation of "microbiological resistance." ECOFFs are preferred for surveillance since they permit the identification of small changes in bacterial susceptibility, which may indicate emerging resistance and allow appropriate control measures to be considered at an early stage. The concentration ranges used in the testing ensure that both the ECOFF and the clinical breakpoints (CBP) are included, making comparability of results with human data possible.

Since the implementation of the new monitoring prescribed by Decision 2013/652/EU, two EUSR-AMR have been published: data on AMR in bacteria from broilers, fattening turkeys and meat thereof were collected by Member States in 2014 *(5)*, while similar data from fattening pigs and bovines younger than one year of age were collected in 2015 *(6)*.

Results from the monitoring indicate that resistance to commonly used antimicrobials in food-producing animals are usually high (20–50%), very high (50–70%) or extremely high (more than 70%) in most Member States. For example, in *Salmonella* spp. and indicator *E. coli* isolates from most animal species and meat thereof, resistance to ampicillin, tetracyclines and sulfonamides was frequently detected. In addition, resistance to fluoroquinolones, which according to the World Health Organization (WHO) are critically important antimicrobials (CIAs) in human medicine *(33)*, was also high or extremely high in *Salmonella* spp., *E. coli* and *Campylobacter* spp. isolated from most animal species, especially in poultry *(Table 1)*. More reassuring findings concern the level of resistance to other CIAs tested (macrolides, 3rd- and 4th-generation cephalosporins), which was generally low (1–10%) in all bacterial species and animal species, with few exceptions, especially for resistance to macrolides in pigs and sometimes in broilers. Interestingly, very low (0.1–1%) levels of co-resistance to different CIAs were detected, indicating that treatment options would remain available to treat possible invasive infections originating from those strains, again with some exceptions in broilers. In addition, the introduction of the revised panels of antimicrobials to be tested in the new legislation, which include colistin, was timely, preceding recent reports of emergence of transferable colistin and erythromycin resistance in Asia in 2015. Overall, resistance to colistin was observed at low levels in all animal species.

To be noted is the great variability of the levels of resistance in the different EU Member States. The last EUSR-AMR published *(6)* showed that the proportion of isolates of indicator *E. coli* from fattening pigs that are fully susceptible to all antimicrobials tested tend to decrease as one moves from Northern to Southern European countries *(Fig. 1)*. This may reflect different levels in the consumption of antimicrobials across countries.

In the past few years, the first data became available in relation to presumptive ESBL-/AmpC-/carbapenemase production in *Salmonella* spp. and *Escherichia coli*. Occurrence of ESBL-/AmpC-producers was low in all species. In 2015, for the first time, prevalence data was collected through specific monitoring performed on cecal *E. coli* isolates from fattening pigs and calves, and from derived meat, after culture in selective media containing cefotaxime (1 mg/l). This method is more sensitive than the non-selective culture methods *(18)* and is able to estimate the proportion of samples contaminated with presumptive ESBL-/AmpC-producing indicator *E. coli* among the samples collected, thus providing additional information compared with occurrence data originating from random testing of isolates. Variable prevalence rates of ESBL-/AmpC-producers were observed among countries, higher in cecal samples than in meat. Carbapenemase-producing *E. coli* were detected in single samples of pig meat and from fattening pigs from two Member States. In 2016, the specific monitoring was carried out also in poultry, and data will be reported in the next EUSR-AMR, to be published in 2018.

Since 2015, a yearly reference testing exercise has been established in collaboration with the European Reference Laboratory for Antimicrobial resistance (EURL-AR)

TABLE 1. Occurrence of resistance to selected antimicrobials in *Salmonella* spp. and indicator *Escherichia coli* in food-producing animals and food in 2014/2015, according to EU AMR monitoring as set by Decision 2013/652/EU, using harmonized ECOFFs. Values reported in the table are EU total values, including results from all reporting Member States. There is variability in the number of reporting Member States and in the occurrence of resistance within each Member State (source: *5, 6*)

	Occurrence of resistance (%)							
	Salmonella spp.				*Escherichia coli*			
	AMP	SXT	TET	CIP	AMP	SXT	TET	CIP
Broilers	19.1	45.1	40.4	53.5	58.6	53.1	50.1	65.7
Laying hens	8.8	10.6	11.4	15.9	n/a	n/a	n/a	n/a
Fattening turkeys	58.0	50.4	68.3	65.8	69.0	51.1	70.9	50.3
Fattening pigs	45.3	52.6	53.5	4.7	39.3	44.2	54.7	10.5
Calves	40.0	51.3	50.0	2.5	31.0	36.6	45.4	11.4
Pig carcasses	44.7	48.5	49.1	4.3	n/a	n/a	n/a	n/a
Broiler meat	9.4	27.0	21.2	42.6	39.2	38.1	26.5	28.0
Turkey meat	30.1	27.0	64.6	24.3	70.5	48.4	61.6	40.5
Pig meat	44.7	48.5	49.1	4.3	n/a	n/a	n/a	n/a
Bovine meat	40.0	50.0	51.3	2.5	n/a	n/a	n/a	n/a

AMP: ampicillin; SXT: sulfamethoxazole; TET: tetracycline; CIP: ciprofloxacin; n/a: not available

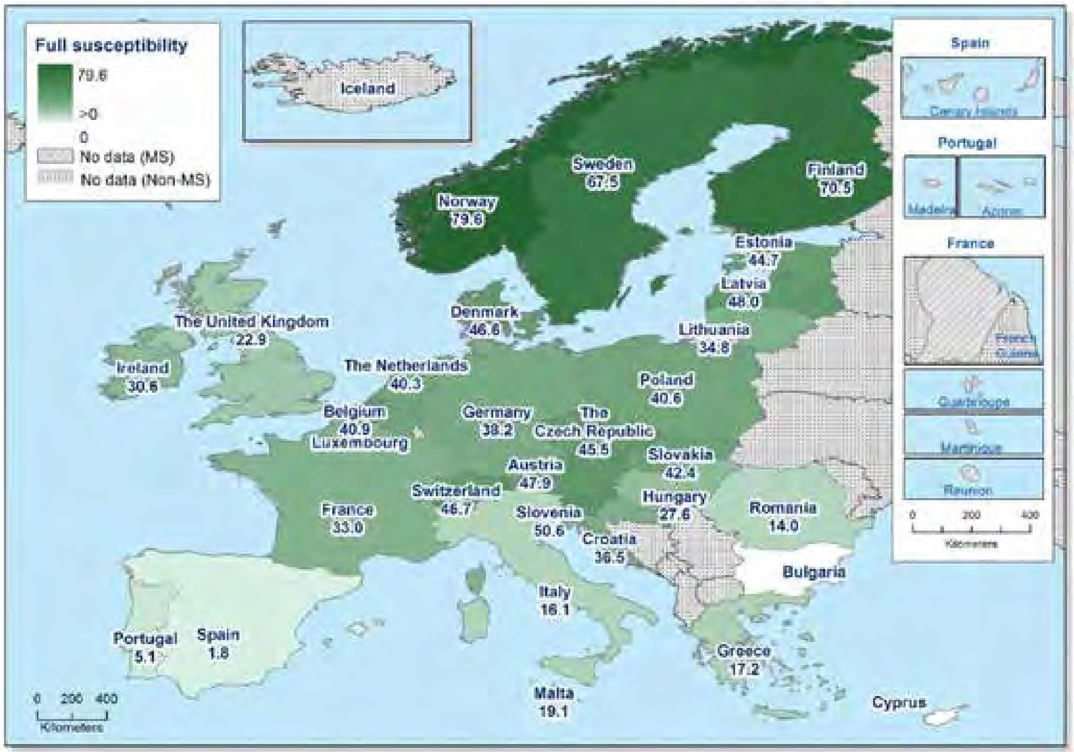

FIGURE 1. Spatial distribution of full susceptibility to the panel of antimicrobials tested among indicator Escherichia coli *from fattening pigs in EU reporting Member States, 2015, using harmonized ECOFFs (source: 6)*

and EU Member States, to support the quality of the data included in the report as well as to explore the potential of whole genome sequencing (WGS) for AMR surveillance. Within this exercise, selected isolates for which Member States have reported AMR data to EFSA are submitted to WGS analyses performed by the EURL-AR to investigate the correlation between genotypes and phenotypes, detection of emerging resistance mechanisms and detection of resistant clones.

Use of AMR monitoring data

AMR data collected by Member States and analyzed by EFSA are useful to assess and follow up the AMR epidemiological situation over the years in food-producing animals and food in EU Member States, and can be compared with similar data originating from humans, which are also presented and discussed in the EUSR-AMR. In addition, they allow further analysis on the possible associations between AMC in food-producing animals and humans. In 2011, the five-year European Commission Action Plan against the rising threats from AMR introduced a set of measures to further strengthen surveillance, monitoring and data collection not only of AMR but also of AMC, improving the scope and coverage in both human and veterinary medicine. In the EU, the monitoring and surveillance of AMR and AMC in humans are currently coordinated by the ECDC, whereas the monitoring of AMC in food-producing animals is coordinated by EMA. EFSA, jointly with ECDC and EMA, has published two Joint Interagency Antimicrobial Consumption and Resistance Analysis (JIACRA) reports that investigate the associations between AMC and AMR *(8, 9)*.

The first JIACRA report covered data from the years 2011–2012, while the second one covered data from the years 2013–2015. Considering both datasets, positive associations were observed between AMC and AMR within animals and humans, between AMR in animals and humans, and between AMC in animals and AMR in humans for certain antimicrobials and bacteria. For example, in relation to food-producing animals, statistically significant associations were observed between consumption of and resistance to fluoroquinolones, tetracyclines and polymixins in *E. coli*. Consumption of macrolides was also significantly associated with resistance in *Campylobacter coli*. In addition, in an attempt to account for the co-selection phenomenon, a statistically significant negative association was consistently detected between the total AMC and the occurrence of complete susceptibility in indicator *E. coli* from food-producing animals, defined as susceptibility to all the antimicrobial classes tested in the harmonized panel prescribed by legislation. In the second JIACRA report *(9)*, multivariate analyses provided a unique approach to assess the contributions of AMC in humans and animals and AMR in bacteria from animals to AMR in bacteria from humans.

Multivariate analyses demonstrated that 3rd- and 4th-generation cephalosporin and fluoroquinolone resistance in *E. coli* from humans was associated with corresponding AMC in humans, whereas resistance to fluoroquinolones in *Salmonella* spp. and *Campylobacter* spp. from humans was related to consumption of fluoroquinolones in animals. Overall, the JIACRA results suggest that from a One Health perspective, there is potential in both the human and animal sectors to further develop prudent use of all antimicrobial classes and thereby reduce AMR.

The AMR data collected may also be helpful when investigating the effectiveness of management measures taken or the general impact of an AMR national/local action plan and efforts towards the reduction of AMC and AMR in both animals and humans. To help and simplify the interpretation of the results from the AMR monitoring, available data might be selected or combined in indicators, which can give a general idea of the progress of the epidemiological situation. Recently, EFSA, ECDC and EMA jointly developed indicators that can be used to monitor the progress of Member States towards the reduction of AMC and AMR in both humans and food-producing animals, based on the AMR and antimicrobial sale data already collected by Member States and analyzed by the three EU agencies *(34)*. Examples of proposed indicators to assess AMR in human medicine include the proportion of *Staphylococcus aureus* that are resistant to meticillin (MRSA) and the proportion of *E. coli* that are resistant to 3rd-generation cephalosporins. These two pathogens are of major public health importance. For veterinary medicine, an example indicator is the proportion of commensal *E. coli* from food-producing animals that are completely susceptible to all antimicrobials tested in the harmonized panel prescribed by legislation. In terms of AMC, some of the suggested indicators are the total consumption of antimicrobials in humans (limited to antibacterials for systemic use) and the overall sales of veterinary antimicrobials. Notwithstanding the need to analyze the underlying data to fully understand the epidemiological situation in the different countries and animal species, and the limitations that such high-level indicators may have in representing the real situation, these are expected to constitute a useful tool for risk managers to monitor the progress made by Member States in these fields.

SCIENTIFIC ADVICE TO THE RISK MANAGER

Scientific advice and AMR risk assessments

EFSA is providing regulators with scientific and technical advice on AMR, as a basis of informing related risk-management decisions. Over recent years, EFSA has been consulted by the European Commission on a number of topics and has also taken the initiative to investigate AMR-related emerging risks and topics of particular concern for public health and food safety. For example, scientific opinions were adopted by the EFSA Panel on Biological Hazards (BIOHAZ Panel) on MRSA *(13)*, ESBL-/AmpC-producing and carbapenemase-producing bacteria in food-producing animals and food *(22, 23)*.

MRSA first emerged in hospital environments in the 1970s, and since then its diffusion worldwide has increased, so that it has become a serious health problem in hospitals. More recently, MRSA was isolated from people in the general community who had no epidemiological connections to hospitals. In addition, strains of MRSA associated with animals have been also identified, from both food-producing animals and pets. In 2009, EFSA assessed the public health significance of MRSA in animals and foods *(13)*. The EFSA BIOHAZ Panel concluded that livestock-associated MRSA represented only a small proportion of all reported MRSA infections in the EU, with significant differences between Member States. The assessment reviewed control options that could be considered to minimize the risk of transfer of food-associated and animal-associated MRSA to humans, and concluded that since the most important routes of transmission to humans are through direct contact with live animals and their environments, the most effective control options would be pre-harvest measures, including good husbandry practices, HACCP, good hygienic and manufacturing practices (GHP, GMP), and possible restrictions of the movements of livestock. It also recommended the application of basic hygienic measures before and after contact with horses and companion animals.

In the 2000s, beta-lactamases also emerged in Gram-negative bacteria, including ESBL and AmpC, which confer resistance to a variety of beta-lactam antimicrobials, including penicillins, cephalosporins and monobactams. More recently, carbapenemases have also emerged, conferring resistance to carbapenems, which are generally used to treat serious infections caused by multidrug-resistant Gram-negative bacteria. Two EFSA opinions assessed public health risks related to ESBL-, AmpC- and carbapenemase-producing bacteria in food-producing animals and food, and related control options *(22, 23)*. The opinions highlighted that despite the fact that few studies present clear evidence of direct transmission of these bacteria from food-producing animals or food to humans, the existence of common clones provide indirect evidence of this transmission. Various control options were identified, but in both opinions, because of a lack of comparative efficacy and efficiency of individual measures, their prioritization was deemed to be very difficult. The assessment of the impact of control measures aimed at controlling carbapenemase-producing bacteria was particularly difficult, because of the very low expected prevalence of those bacteria in the food chain. The EFSA BIOHAZ Panel indicated that decreased frequency of use of antimicrobials in animal production in the EU is of high priority for the control of the emergence and spread of resistance and co-resistance phenomena, and indicated that stopping the use of 3rd- and 4th-generation cephalosporins, or restricting their use to specific circumstances, would be a highly effective option. Carbapenems are not licensed for use in food-producing animals in the EU, and the continuation of this prohibition was identified as an effective measure to minimize the emergence and spread of resistance to these antimicrobials from the animal reservoir. The need for implementing strict measures or prohibitions of off-label use of those substances was also mentioned. Since carbapenemase-producing genes and genes encoding resistance to certain heavy metals such as zinc are sometimes linked, the use of compounds containing such elements should be minimized. Together with these options, other measures aimed at controlling the risks of spread of those bacteria through the food chain were discussed, such as biosecurity measures for the containment of resistant bacteria at the farm level and during transport of animals and products thereof, and post-harvest hygienic and decontamination measures having effect at later stages of the food chain. Measures aimed at minimizing the risks of transmission of antimicrobial-resistant bacteria to humans through pathways other than food were also considered.

As already pointed out, the misuse and abuse of antimicrobials in food-producing animals can lead to the emergence of AMR bacteria in animal populations, which can contribute to an increase of the AMR problem in humans as well. That is why, among measures taken to fight against AMR, the European Commission developed and published Guidelines for the prudent use of antimicrobials in veterinary medicine *(2, 3)*. As a follow-up action, the European Commission requested EFSA, jointly with EMA, to produce a scientific opinion about measures to reduce the use of and the need to use antimicrobials in animal husbandry in the EU, and the resulting impacts on food safety. The resulting scientific opinion (RONAFA Opinion) *(27)* reviewed available measures and highlighted a series of reduction strategies that have been implemented successfully in some Member States and that could be integrated into national action plans and implemented across the EU. These would be aimed first of all at the direct reduction of the consumption of antimicrobials, for example by setting targets for the reduction of their use, by increasing the responsibility and accountability of veterinarians prescribing antimicrobials, and by limiting the use of antimicrobials to those situations where they are absolutely needed, in particular eliminating their use for prophylactic purposes. In addition, the RONAFA opinion recommended considering additional measures aimed at replacing antimicrobials with alternatives. The opinion reviewed and discussed a number of alternatives which have been shown to yield good results in the improvement of animal health parameters during experimental studies, such as probiotics, bacteriophages, organic acids, immunomodulators, teat sealants, etc. Since some of these products are not yet commercially available and some have shown to be promising, the opinion also recommended giving new impetus to the scientific research on these and other alternatives, and designing an EU legislative framework that would stimulate their development and clarify the pathway for their approval. Finally, within this opinion, the need to rethink the livestock production system was discussed. Improving disease prevention and control measures on farms would allow reducing the introduction and spread of animal diseases and contribute indirectly to reduction of the use of antimicrobials. Benchmarking between farms and prescribing veterinarians in relation to use and prescription of antimicrobials would also allow identifying critical situations and switching to farming conditions that would be sustainable with reduced use of antimicrobials. Finally, the opinion highlighted the role of continuing education for all actors involved in animal farming and management, such as farmers and veterinarians.

The RONAFA Opinion also recommended the development of indicators suitable for monitoring and detecting trends in the levels of key drug-resistant microorganisms in humans, food-producing animals and food derived thereof, and of AMC. This is another area of recent work, following to the request by the European Commission to ECDC, EFSA and EMA, already mentioned *(34)*.

The use of colostrum or milk potentially containing residues of antimicrobials is not fully harmonized within the EU. In many Member States these products may be used to feed calves originating from the same farm. In 2016, the European Commission requested that EFSA also provide scientific advice on the risk of the development of AMR due to these feeding practices. The EFSA BIOHAZ Panel *(24)* concluded that consumption of milk from cows receiving antimicrobial treatment during lactation, and milked during the treatment or the withdrawal period, would lead to increased probability of fecal shedding of antimicrobial-resistant bacteria by calves. A range of possible options exists for restricting the feeding of such milk to calves, which could target, for example, the highest-priority critically important antimicrobials.

Resistance to polymyxins is also an important public health issue, attention to which particularly rose after the discovery of new horizontally transferrable resistance mechanisms to colistin, and the detection of plasmids carrying resistance genes in food-producing animals and food thereof *(31)*. EFSA has provided support to EMA in reviewing previous advice on the impact and need for colistin use for human and animal health *(26)*. Considering the importance of colistin for treatment of human infections resistant to other antimicrobials, this updated advice recommended that all countries reduce the use of polymyxins in livestock as much as possible, and suggested target levels that could be set for the reduction of the use of colistin in three to four years.

Scientific advice on regulated products

EFSA is also involved in the assessment of applications for certain regulated products and substances before they can be approved for use in food and feed in the EU. AMR-related concerns are taken into consideration when applications are assessed in a number of areas, such as feed additives, chemical decontamination of foods of animal origin and genetically modified organisms (GMOs).

As an example, as provided for in Regulation (EC) No 429/2008, strains of microorganisms intended for use as feed additives or as a source of feed additives shall not contribute further to the reservoir of AMR genes already present in the gut flora of animals and the environment. Consequently, all strains of bacteria shall be tested for resistance to antimicrobials in use in human and veterinary medicine. To allow differentiation between resistant and susceptible microorganisms, the FEEDAP Panel produced a Guidance on the assessment of bacterial susceptibility to antimicrobials of human and veterinary importance *(25)*, currently under revision. Where resistance is detected, the genetic basis of the resistance and the likelihood of transfer of resistance to other gut-inhabiting organisms shall be established. Strains of microorganisms carrying an acquired resistance to antimicrobials shall not be used as feed additives, unless it can be demonstrated that resistance is a result of chromosomal mutations and it is not transferable.

ONE HEALTH APPROACH

AMR is a global problem. As already mentioned, humans can acquire AMR bacteria and AMR determinants from many different sources and routes, including other humans, food-producing animals, pets and the environment. Therefore, it needs to be approached from different angles, and successful measures can be derived only from collaboration across different sectors, including the human and veterinary ones, in accordance with the One Health approach, as stated by all major international organizations *(29, 30, 32)* and by the European Commission and the Council of the EU *(4, 28)*.

EU agencies responsible for different AMR aspects closely collaborate in the One Health spirit, to analyse the AMR challenge from different angles and provide the EU risk manager and Member States with scientific advice that tackles AMR challenges from different perspectives. For example, when providing advice on measures to be put in place to reduce the use of and need to use antimicrobials in food-producing animals, EMA and EFSA *(27)* emphasize that national strategies and action plans should be developed by the Member States, taking into account the One Health aspects of AMR to integrate actions on the veterinary and human sides. Several other examples of EU interagency collaboration exist, some of which have been mentioned in this paper, with regard to both the collection and analysis of AMR monitoring data from humans and animals *(5, 6, 8, 9)* and joint assessments *(10, 11, 26, 27)*.

Given the rapidity with which AMR-bacteria can spread internationally, collaboration at the global level is also crucial to addressing the fight against AMR. Therefore EFSA is also involved in international initiatives, such as the activities of the Transatlantic Task Force on Antimicrobial Resistance (TATFAR) and Codex Alimentarius. For example, EFSA has provided ad hoc scientific advice to the European Commission in relation to the possible links between the use of rBST in dairy cows and AMR, discussed by the Codex Joint Expert Committee on Food Additives *(20)*.

To support and follow new developments on the field, EFSA is also funding research projects dealing with antimicrobial resistance and use of WGS (e.g., ENGAGE, INNUENDO) and is a member of the external advisory boards of EU-funded research projects dealing with AMR (e.g., EFFORT, COMPARE).

RISK COMMUNICATION

Besides risk assessment and scientific advice, EFSA is also responsible for risk communication on food safety topics. Consumers also play an important role in the AMR fight, and awareness on the part of society of AMR can lead to changes in attitudes and behaviors that can have a positive impact on AMR *(27)*. Therefore EFSA is investing in providing clear communication on this aspect by means of news stories and press releases, as well as interactive tools to inform the general public on the results of its risk assessments, such as videos and infographics, also in collaboration with other EU agencies, which are available on the EFSA Web site.

FINAL CONSIDERATIONS

AMR is a global threat, and resistance among bacteria has increased in recent decades, following misuse and abuse of antimicrobials in both food-producing animals and humans. This poses a serious risk to public health, and there is a need for prompt action against this threat at all levels, in accordance with the One Health approach.

EFSA has a prominent role in the AMR area in the EU and at the international level. In close cooperation with other EU agencies, such as ECDC and EMA, EFSA provides scientific and technical advice to allow risk managers to make science-based decisions to fight against AMR.

EFSA also has an active role in the design of AMR monitoring in food-producing animals and food, advising Member States on the implementation of monitoring, collecting and analyzing related data, as well as performing AMR monitoring at the EU level. Monitoring the AMR situation in food-producing animals and food and incrementing its implementation is crucial to identifying priority areas for action, detecting emerging threats and assessing the effectiveness of the measures taken. Further development of harmonized systems for monitoring AMC and AMR is recommended, integrating data from humans, food-producing animals and derived food, and the environment.

It is also crucial that all EU Member States have national strategies against AMR that are implemented through action plans, integrating actions on the veterinary and human side, in accordance with the One Health approach, and involving all sectors throughout the food chain. EFSA can also play a central role in the EU, providing scientific advice to Member States and the European Commission to set science-based strategies to reduce the development of AMR.

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