❖Facing to regional and global AMR challenges, EU stands at the forefront for addressing AMR

❖No single, isolated action could provide an adequate solution

❖Resistant bacteria and infectious diseases know no borders

❖No individual MS can tackle the problem on its own

❖EU has position to act given its commitment to a high level of human health protection

HISTORICAL OVERVIEW:

➤ 2001. recognized the importance of AMR – Community Strategy against Antimicrobial Resistance – first policy instrument addressing AMR at European level comprising:

o Surveillance

o Prevention and control

o Research and product development

o International cooperation

➤ 2011. the policy was reinforced – Action Plan using "One health" holistic approach addressing AMR in both humans and animals

➤ 2016. A new comprehensive EU Action was requested by MS and it is built upon the evaluation of the previous, EU roadmap and open public consultations

Annex 5 -- Ratio of the consumption of broad-spectrum to the consumption of narrow-spectrum antibacterials (enacompassing penicillins, cephalosporins and macrolides)

Country	2011	2012	2013	2014
Austria	7.79	8.09	8.25	8.17
Belgium	64.32	79.17	80.12	79.92
Bulgaria	8.01	10.07	11.83	17.7
Croatia	6.05	8.15	7.89	8.75
Cyprus**	29.74	28.45	36.87	37.87
Czech Republic	4.03	5.43	4.79	5.11
Denmark	0.53	0.59	0.62	0.63
Estonia	9.98	10.54	11.6	11.9
Finland	0.88	0.82	0.73	0.73
France	46.03	50.63	47.64	40.21
Germany	5.01	4.94	5.66	5.62
Greece	133.58	258.32	318.32	606.81
Hungary	19.66	21.71	25.74	37.55
Iceland**	1.76	1.68	2.08	1.99
Ireland	6.26	6.46	5.68	5.07
Italy	140.15	158.44	171.64	184.26
Latvia	7.66	11.5	11.75	12.35
Lithuania	4.72	10.54	11.69	10.49
Luxembourg	38.23	47.38	53.42	52.42
Malta	142.7	162.07	153.27	180.36
Netherlands	7.4	7.82	7.84	7.77
Norway	0.21	0.23	0.23	0.21
Poland	57.63	36.93	34.87	29.02
Portugal	32.26	34.85	34.26	37.88
Romania**	6.45	8.39	11.03	11.88
Slovakia	8.77	8.85	9.84	10.33
Slovenia	3.36	3.22	3.54	3.96
Spain	63.1	65.69	74.68	76.13
Sweden	0.17	0.17	0.2	0.37
United Kingdom	1.15	1.35	1.5	1.64

Source: ESAC database http://ecdc.europa.eu/en/healthtopics/antimicrobial_resistance/esac-net-database

THE NEW EU ONE HEALTH ACTION PLAN AGAINST AMR - 2017

Goal: to preserve the possibility of effective treatment of infections in humans and animal providing a framework for continued, more extensive action to reduce the emergence and spread of AMR and to increase the development and availability of new effective antimicrobials inside and outside EU built on three pillars:

1. Making the EU a best practise region
2. Boosting research, development and innovation
3. Shaping the global agenda

1. Making the EU a best practice region

➢ **Better evidence and awareness of the challenges of AMR:** Strengthen One Health surveillance and reporting of AMR and AMU (review EU legislation on monitoring of AMR, reporting diseases in humans, identify and assess zoonotic bacteria, improve AMR detection in humans, consider AMR monitoring in environment)

➢ **Benefit from the vast evidence-based analysis and data** (provide data on possible link between consumption of antimicrobials and occurrence of AMR in humans and food producing animals, support the development of a model to assess the economic burden of AMR on people and to estimate the cost-effectiveness of national policies to reduce it

➢ **Increase awareness and understanding** (provide insight into public use and knowledge through available means, support national awareness raising, contribute to the annual European Antibiotic Awareness Days)

➢ **Better coordination and implementation of EU rules to tackle AMR** (make available regular info on AMR at MS and EU level, support national One health action plans, launch joint actions, make increased use of EU Health Security Committee and Commission Working group on AMR in vet. and food areas, seek co-fund and collaboration with WHO to help EU MS to develop and implement One health AMR National Plans, better implementation of EU rules and monitoring of implementation, training programs for MS competent authorities (BTFS)

➢Better prevention and control of AMR (strengthen infection prevention and control measures in hospital environment, vulnerable groups, promote uptake of vaccination in humans, promote animal husbandry systems and feeding to support good animal health and welfare, promote prudent use of antimicrobials by reserving antimicrobials for human use, reporting the sales and use of antimicrobials, develop guidelines for prudent use in human medicine, assist MS implementation EU guidelines for prudent use in vet. medicine, encourage EMA to review info on benefits and risk of older antimicr.agents

➢Better addressing the role of the environment (EU strategic approach to pharmaceuticals in the environment, maximise use of data from existing monitoring to improve knowledge, reinforce role of the Scientific Committee on Health and Environmental Risks (SCHER)

➢Stronger partnership against AMR and better availability of antimicrobials (collaboration among key stakeholders in human and animal health, food, water and environmental sector to encourage the responsible use of antimicrobials and appropriate handling of waste material, ensure availability of human and vet antimicrobials and provide incentives to increase the uptake of diagnostics, antimicrobial alternatives and vaccines; reduce the scope for falsified medicines, discuss the availability of vet antimicrobials in the Veterinary Pharmaceutical Committee

2.BOOSTING RESEARCH, DEVELOPMENT AND INNOVATION ON AMR

➤**Improve knowledge on detection, effective infection control and surveillance** (support research into prevention of development and spread of AMR, in understanding the epidemiology of AMR, new tools for early detection of resistant pathogens in humans and animals and into new eHealth solution to improve prescription practices

➤**Develop new therapeutics and alternatives for humans and animals** (support SMEs in R&D towards innovative and alternative therapeutic approaches in treatment and prevention of bacterial infection, sharing of antimicrobial research data among stakeholder, support establishment of European-wide sustainable clinical network)

➤**Develop new preventive vaccines** (support research into development of new effective vaccines for humans and animals, increasing knowledge base concerning the barriers that influence the wider use of vaccination in medical and vet practise)

➤**Develop novel diagnostics** (support research into development of new diagnostic tools in particular on-site tests, IT solutions in developing tools for diagnosing, encourage the uptake of diagnostics in both **medical and vet practise**

➤**Develop new economic models and incentives** (increase the evidence for understanding the societal costs and benefits of different strategies for fighting AMR, developments of new economic models for development of therapeutics, vaccines and diagnostics, encourage MS to explore results of EU projects etc.

➤**Close knowledge gaps on AMR in the environment and on how to prevent transmission** (support research on release of resistant microorganisms and their spread, explore risk assessment tools, monitoring and methods to degrade antimicrobials in wastewaters and environment)

3. SHAPING THE GLOBAL AGENDA

➢ **A stronger EU global presence** -contribute to normative work of WHO, OIE, FAO, Codex Alimentarius on development of international frameworks and standards/norms/guidelines related to AMR, reinforce technical cooperation with WHO in the WHO Global Action Plan on AMR, support international Conference on harmonisation of technical requirements for registration of pharmaceuticals for human and vet use, international conference on harmonisation, work to raise polical attention to AMR ACTION in the UN forums, G7 and G20, continue collaboration within TATFAR (EU, USA, Canada, Norway), promote international regulatory convergence between EMA, FDA and Japan Pharmaceutical and Medical Devices Agency (PMDA) on plans for new antimicrobials

➢ **Stronger bilataeral partnership for stronger cooperation** -advocate EU standards and measures for tackling AMR in trade agreement and incoporate them into cooperative arrangements in trade agreement, engage with major global players and strategic countries (India, China, Brasil), support capacity building and legislation implementation in candidate and neighbouring countries related to AMR

➢ **Cooperation with developing countries-** contribute to reduce AMR through infectious diseases programmes, assist in development of national strategy in food safety and animal helth through organising training workshops

➢ **Developing a global research agenda** – improve global coordination of research activities, support estabishment of virtual institutes, support subSaharian Africa in collaborative research, foster international research collaboration on AMR in animal health sector

IMPLICATIONS FOR TRADING PARTNERS

1. The new Plan will propose measures to help Member States implement antimicrobial stewardship practices ensuring an optimal use of antimicrobials. Furthermore, the Commission proposals for new Regulations on veterinary medicinal products and on medicated feed, currently undergoing the ordinary legislative procedure, contain a set of requirements addressing the threat of AMR, including provisions aiming at responsible use of veterinary antimicrobials.

2. The Commission is gathering information from the main EU trading partners, on their policies regarding the fight against the rise of AMR. These include actions taken nationally to monitor the incidence of AMR in bacterial isolates from animals and meat. This information will be used to inform the Commission's future activities in this area.

3. The Commission will reinforce its engagement and collaboration with multilateral organisations, such as the WHO, OIE and the FAO, so as to contribute towards their normative work on the development of international standards related to AMR.

This includes the work of the Task Force on AMR recently established by the Codex Alimentarius. The Commission will also promote the inclusion of AMR on the agenda of the next G20 Summit**. The Commission now systematically proposes to include the issue in all new Free Trade Agreements being negotiated.**

NATIONAL ACTION PLAN ON AMR – EXAMPLE OF CROATIA

➢ 2006 - based   on the recommendation of the WHO, ECDC and European Councile, Goverment issued decision on establishment of the interdisciplinary group ISKRA (interdisciplinary session for control of AMR)

➢ The first 5 year NAP on AMR was put in force for period 2009-2014 and currently is in force the second NAP (2015-2020)

➢ Comprehensive analysis showed that Croatia is a country with AMU under the average in EU and the significant efforts should be engaged into training and awareness raising both in those who prescribe the AM and users regardless in human or veterinary medicine
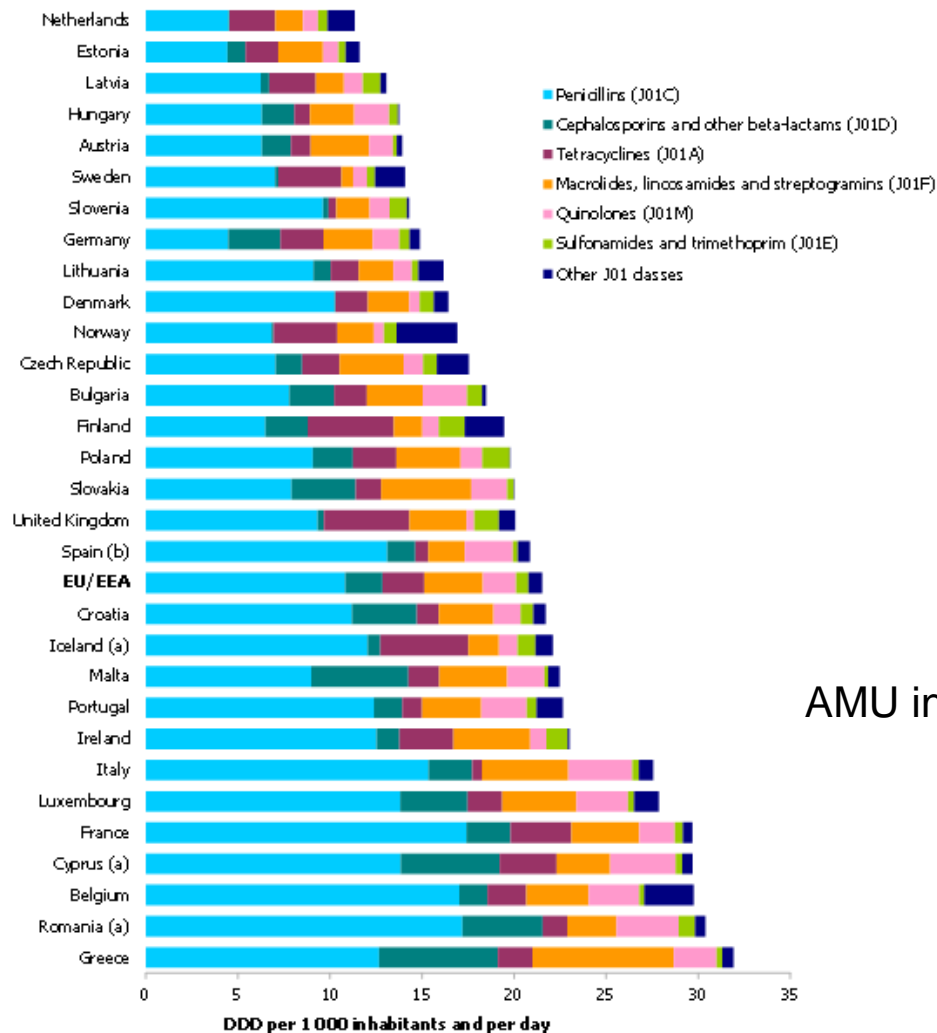
AMU in EU countries in 2012

NATIONAL ACTION PLAN

Main actions foreseen:

- ❑ Surveillance of the antimicrobial resistance of the bacteria in Croatia (in humans and animals by harmonizing the testing methods, reporting to competent EU agencies- EFSA or ECDC, particularly in zoonotic bacteria)
- ❑ Tracing of the antimicrobials consumption
- ❑ Promotion of responsible use of antimicrobials (education of the students, preparing guidelines for responsible use, diagnostics methods development and improvement, "antimicrobial stewardship", control of the sale)
- ❑ Control of spreading the resistant bacterial strains (control of hospital infection, promotion of vaccination against bacterial diseases of humans and animals, biosecurity measures implementation in animal farming)

❑ Awareness raising on the adverse effects of excessive use of antimicrobials by organizing different awareness raising campaigns in schools and universities, among farmers and by promoting the 18th of November as European Antibiotic Awareness Day,

❑ Support to the scientific activities aiming to the research in the field of the AMR by Ministry of Health, Agriculture and Sciences (studies of the bacterial resistance mechanisms, its spreading, novel antimicrobials, development of new diagnostic methods leading to effective treatments, creating new methods of specific immunization and fostering the innate immunity

INSTITUTIONS INCLUDED INTO IMPLEMENTATION OF NAP

- Ministry of health
- Ministry of agriculture
-     - Veterinary and food safety directorate
- Ministry of sciences
- Reference centre of Ministry of health for monitoring of AMR
- Clinics for infectious diseases
- Croatian Academy of Medical Sciencies, Group for AMR monitoring
- Croatian Medical Association
  - ✓ Division for clinical microbiology
  - ✓ Division for infectious diseases
  - ✓ Division for chemotherapy
  - ✓ Division for clinical pharmacology
  - ✓ Association of the general practicians
  - ✓ Croatian society of epidemiology

- Public health institution
- Croatian Health Insurance Fund
- Agency for Medicinal Products and Medical Devices
- Medical School University of Zagreb
- Medical School University of Rijeka
- Medical School University of Split
- Medical School of University Josip Juraj Strossmayer in Osijeku
- Faculty of pharmacy and biochemistry University of Zagreb
- Croatian chamber of pharmacists
- Croatian Veterinary Institute
- Veterinary Faculty University of Zagreb
- Authorized veterinary organisations
- Professional veterinary organisations
- Croatian Veterinary Chamber

DIRECTIVE 2003/99/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 17 November 2003

on the monitoring of zoonoses and zoonotic agents, amending Council Decision 90/424/EEC and repealing Council Directive 92/117/EEC

L 303/26 HR Službeni list Europske unije 14.11.2013.

ODLUKE

PROVEDBENA ODLUKA KOMISIJE

od 12. studenoga 2013.

o praćenju otpornosti zoonotskih i komenzalnih bakterija na antimikrobna sredstva i izvješćivanju o tom praćenju

(priopćeno pod brojem dokumenta C(2013) 7145)

(Tekst značajan za EGP)

(2013/652/EU)

efsa
European Food Safety Authority

ANNEX II

Requirements for monitoring of antimicrobial resistance pursuant to Article 7

A. General requirements

Member States must ensure that the monitoring system for antimicrobial resistance provided for in Article 7 provides at least the following information:

1. animal species included in monitoring;
2. bacterial species and/or strains included in monitoring;
3. sampling strategy used in monitoring;
4. antimicrobials included in monitoring;
5. laboratory methodology used for the detection of resistance;
6. laboratory methodology used for the identification of microbial isolates;
7. methods used for the collection of the data.

B. Specific requirements

Member States must ensure that the monitoring system provides relevant information at least with regard to a representative number of isolates of *Salmonella* spp., *Campylobacter jejuni* and *Campylobacter coli* from cattle, pigs and poultry and food of animal origin derived from those species.

CHAPTER III

ANTIMICROBIAL RESISTANCE

Article 7

Monitoring of antimicrobial resistance

1. Member States shall ensure, in accordance with the requirements set out in Annex II, that monitoring provides comparable data on the occurrence of antimicrobial resistance in zoonotic agents and, in so far as they present a threat to public health, other agents.

1. **Technical specification on the harmonized monitoring and reporting of antimicrobial resistance in *Salmonella*, *Campylobacter* and indicator *E.coli* and *Enterobacter***
2. **Manual for notification of zoonosis, causative agents and AMR**
3. **Reporting**

SCIENTIFIC REPORT OF EFSA

Technical specifications on the harmonised monitoring and reporting of antimicrobial resistance in *Salmonella*, *Campylobacter* and indicator *Escherichia coli* and *Enterococcus* spp. bacteria transmitted through food[1]

European Food Safety Authority[2, 3]

European Food Safety Authority (EFSA), Parma, Italy

- o Targeted bacteria
- o Animal species
- o Samples
- o Antimicrobials
- o How to sample
- o How to interprete results

Table 1: Recommendations on the combinations of bacterial species/food animal populations and desirable numbers of isolates to be included in susceptibility testing

| Animal populations	Salmonella			Campylobacter			Indicator commensal E. coli			Indicator commensal enterococci		
	Where to collect	Samples to collect	Target no. isolates	Where to collect	Samples to collect	Target no. isolates	Where to collect	Samples to collect	Target n0. isolates	Where to collect	Samples to collect	Target no. isolates
Monitoring recommended to be performed consistently on a yearly basis												
Laying hens	Farm[a]	boot swabs	170[b]	-	-	-	-	-	-	-	-	-
Broilers	Farm[a]	boot swabs	170[b]	Slaugterhouse	caecal spl.	170[c]	Slaugterhouse	caecal spl.	170	Slaughterhouse	caecal spl.	170
Fattening turkeys	Farm[a]	boot swabs	170	-	-	-	-	-	-	-	-	-
Fattening pigs	Slaugterhouse	caecal spl.	170	Slaugterhouse	caecal spl.	170[d]	Slaugterhouse	caecal spl.	170	Slaugterhouse	caecal spl.	170
Calves under 1 year	Slaugterhouse	caecal spl.	170	-	-	-	Slaugterhouse	caecal spl.	170	Slaugterhouse	caecal spl.	170
Monitoring recommended to be performed on a yearly basis, if production exceeds 10.000 tons/year slaughtered												
Fattening turkeys	-	-	-	Slaugtherhouse	caecal spl.	170	Slaughterhouse	caecal spl.	170	Slaughterhouse	caecal spl.	170
Sheep	Slaughterhouse	caecal spl.	170	-	-	-	Slaughterhouse	caecal spl.	170	-	-	-
Goats	Slaughterhouse	caecal spl.	170	-	-	-	Slaughterhouse	caecal spl.	170	-	-	-
Monitoring recommended to be performed on a regular basis (every 3 years)												
Laying hens	-	-	-	-	-	-	Farm	boot swabs	170	Farm	boot swabs	170
Breeders of Gallus gallus, egg sector	Farm	boot swabs	170	-	-	-	Farm	boot swabs	170	Farm	boot swabs	170
Breeders of Gallus gallus, meat sector	Farm	boot swabs	170	-	-	-	Farm	boot swabs	170	Farm	boot swabs	170
Turkey breeders	Farm	boot swabs	170	-	-	-	Farm	boot swabs	170	Farm	boot swabs	170
Calves under 1 year	-	-	-	Slaughtherhouse	caecal spl.	170	-	-	-	-	-	-
Dairy cattle	Slaughterhouse	caecal spl.	170	-	-	-	Slaughterhouse	caecal spl.	170	Slauhgterhouse	caecal spl.	170
Young bovines (1 to 2 years)	Slaughterhouse	caecal spl.	170	-	-	-	Slaughterhouse	caecal spl.	170	Slaughterhouse	caecal spl.	170

Table 6: Proposed set of antimicrobial substances to be included in AMR monitoring, EUCAST epidemiological cut-off values (ECOFFs) and clinical breakpoints and concentration ranges to be tested in all *Salmonella* and *Escherichia coli* isolates

Antimicrobial	Species	EUCAST values[a] (in mg/L)		Range of concentrations (mg/L)			
		ECOFF	Clinical resistance breakpoint	Current recommendation	New recommendation (no of wells in brackets)		
					Optimal	Advised	Minimum
Ampicillin	*Salmonella*	>8[b]	>8	0.5–64	0.5–128 (9)	1–128 (8)	2–128 (7)
	E. coli	>8	>8	1–128			
Cefotaxime	*Salmonella*	>0.5	>2	0.06–8	0.015–4 (9)	0.03–4 (8)	0.12–4 (6)
	E. coli	>0.25	>2	0.015–2			
Ceftazidime	*Salmonella*	>2	>4	Not included	0.06–8 (8)	0.06–8 (8)	0.25–8 (6)
	E. coli	>0.5	>4	Not included			
Meropenem	*Salmonella*	>0.125	>8	Not included	0.008–16 (12)	0.12–0.25 (2)	0.12–0.25 (2)
	E. coli	>0.125	>8				
Nalidixic acid	*Salmonella*	>16	–	2–256	1–128 (8)	4–128 (6)	4–128 (6)
	E. coli	>16	–	1–128			
Ciprofloxacin	*Salmonella*	>0.064	>1	0.008–8	0.008–16 (12)	0.008–8 (11)	0.03–8 (8)
	E. coli	>0.064[b]	>1	0.004–4			
Tetracycline	*Salmonella*	>8	–	0.5–64	0.5–128 (9)	1–128 (8)	2–128 (7)
	E. coli	>8	–	1–128			
Colistin	*Salmonella*	>2[c]	>2	Not included	0.12–16 (8)	0.5–16 (6)	0.5–16 (6)
	E. coli	>2	>2	Not included			
Gentamicin	*Salmonella*	>2	>4	0.25–32	0.25–32 (8)	0.5–32 (7)	0.5–32 (7)
	E. coli	>2	>4	0.12–16			
Streptomycin	*Salmonella*	>16[b]	–	2–256	2–256 (8)	2–256 (8)	8–256 (6)
	E. coli	>16[d]	–	2–256			
Trimethoprim	*Salmonella*	>2	>4	0.25–32	0.25–32 (8)	0.25–32 (8)	1–32 (6)
	E. coli	>2	>4	0.12–16			
Sulfamethoxazole	*Salmonella*	>256[e]	–	8–1024	4–1024 (9)	8–1024 (8)	32–1024 (6)
	E. coli	>64[b]	–	8–1024			
Chloramphenicol	*Salmonella*	>16	>8	2–256	2–256 (8)	8–256 (6)	8–256 (6)
	E. coli	>16	>8	2–256			

Table 9: Proposed panel of antimicrobial substances to be included in AMR monitoring, EUCAST epidemiological cut-off values (ECOFFs) and clinical breakpoints and concentration ranges to be tested in *C. jejuni* and *C. coli*

| Antimicrobial	Species	EUCAST values[a] (mg/L)		Range of concentrations (mg/L)			
		ECOFF	Clinical resistance breakpoint	Current recommendation	New recommendation (no of wells in brackets)		
					Optimal	Advised	Minimum
Erythromycin	*C. jejuni*	>4	>4	0.5–64	0.25–128 (10)	1–128 (8)	1–128 (8)
	C. coli	>8	NA[b]				
Ciprofloxacin	*C. jejuni*	>0.5	>1	0.06–8	0.06–32 (10)	0.12–16 (8)	0.12–16 (8)
	C. coli	>1	>1				
Tetracycline	*C. jejuni*	>1	NA	0.12–16	0.25–128 (10)	0.5–64 (8)	0.5–64 (8)
	C. coli	>2	NA				
Streptomycin	*C. jejuni*	>4	NA	0.5–32	0.5–256 (10)	1–128 (8)	1–128 (8)
	C. coli	>4	NA				
Gentamicin	*C. jejuni*	>2	NA	0.12–16	0.12–16 (8)	0.12–16 (8)	0.12–16 (8)
	C. coli	>2	NA				
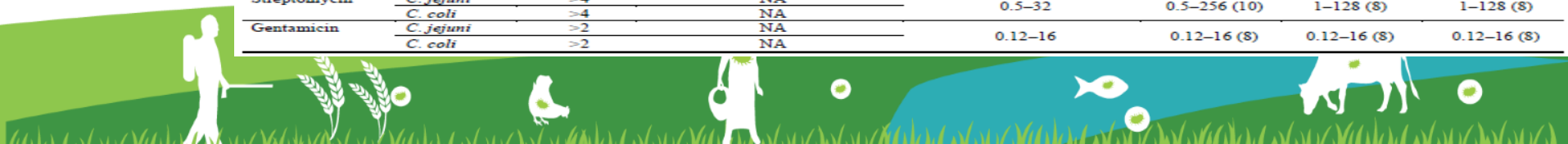
Antimicrobial resistance of indicator bacteria
Escherichia coli isolated from broilers in 2014.

	Indicator *Escherichia coli*	
	N	%R
Ampicilin	170	56.5
Azitromycine	170	1.8
Cefotaxime	170	0.6
Ceftazidime	170	0.6
Chloramphenicol	170	11.2
Cyprofloxacin	170	80.6
Colistine	170	0
Gentamycine	170	5.3
Nalidixic acid	170	74.7
Sulphametoxasol	170	44.7
Tetracycline	170	43.5
Tigeciklin	170	0
Trimethoprim	170	28.8

Antimicrobial resistance of *E. coli* isolated from broilers in 2014. EU / cyprofloxacyne
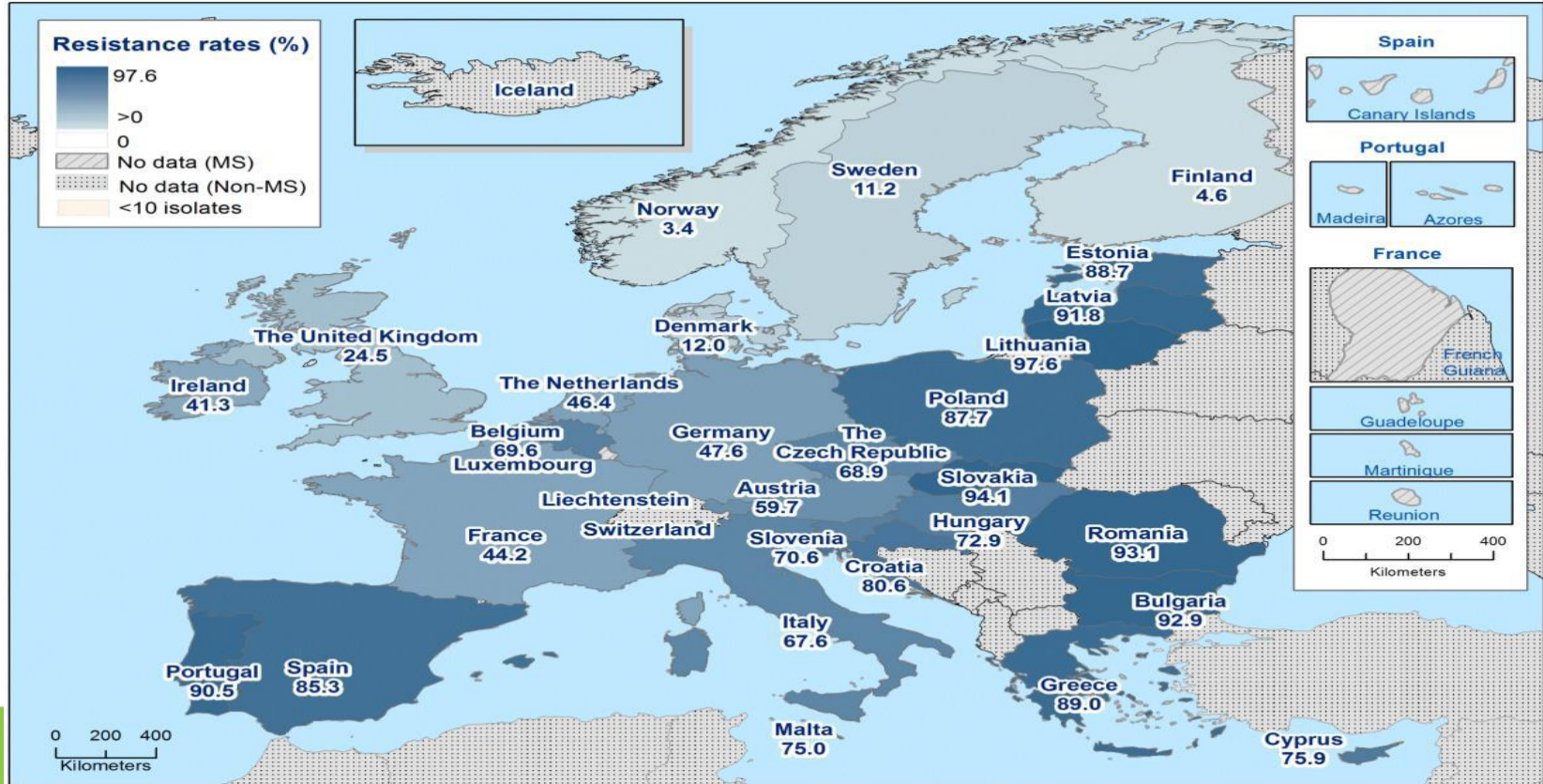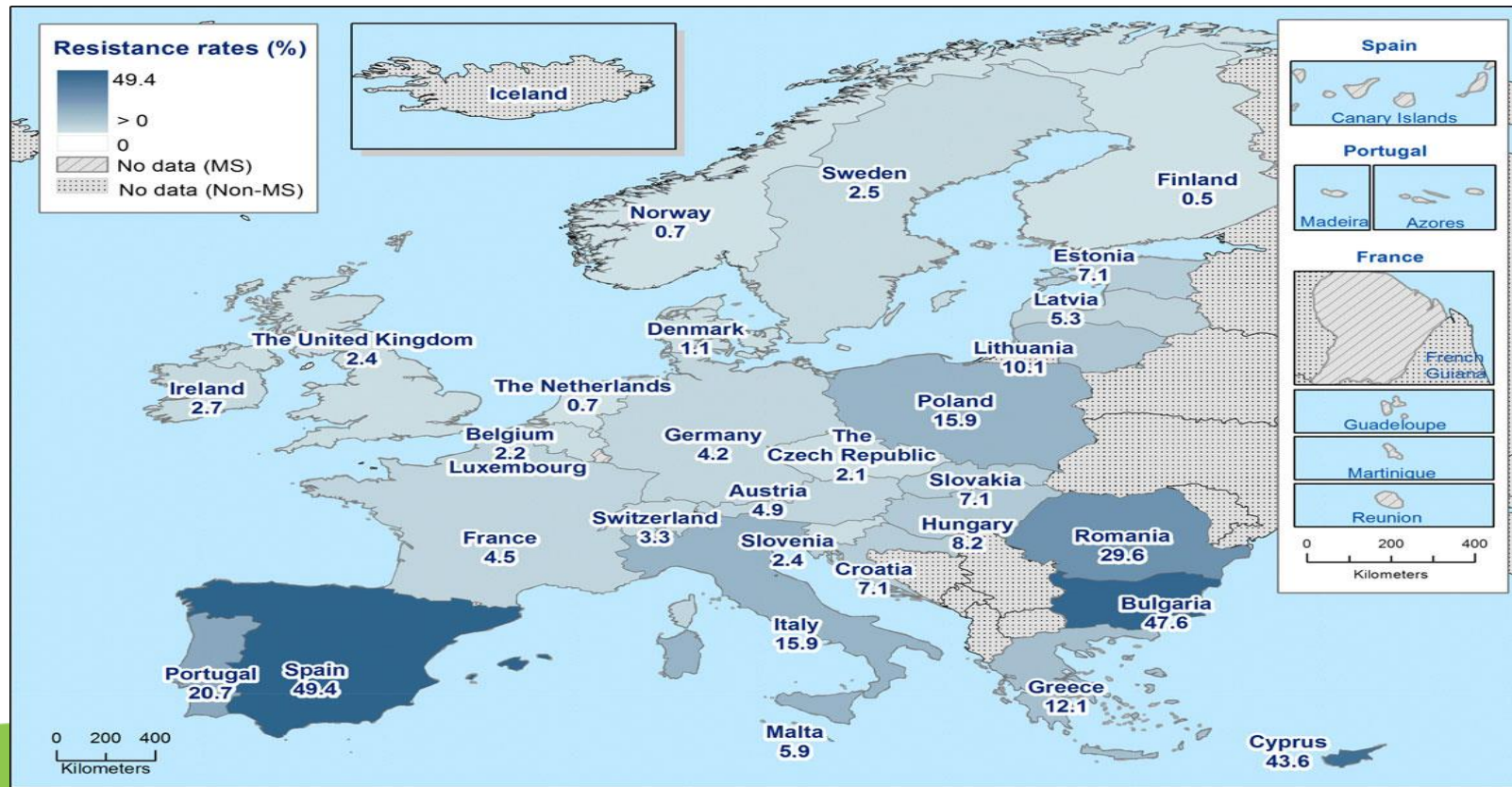
Antimicrobial resistance of indicator bacteria *E. coli* isolated from coecal samples of fattening pigs in 2015.

	Indicator *Escherichia coli*	
	N	%R
Ampicilin	85	32.9
Azitromycine	85	0
Cefotaxime	85	0
Ceftazidime	85	0
Chloramphenicol	85	10.6
Cyprofloxacin	85	7.1
Colistine	85	0
Gentamycine	85	3.5
Nalidixic acid	85	10.6
Sulphametoxasol	85	40.0
Tetracycline	85	56.5
Tigeciklin	85	0
Trimethoprim	85	21.2

Antimicrobial resistance of indicator bacteria *E. coli* isolated from coecal samples of fattening pigs in 2015. - EU / cyprofloksacin

Antimicrobial resistance of indicator bacteria *E. coli* isolated from coecal samples of calves under 1 year in 2015. godine

	Indicatorska *E. coli*	
	N	%R
Ampicilin	85	22.4
Azitromycine	85	0
Cefotaxime	85	0
Ceftazidime	85	0
Chloramphenicol	85	12.9
Cyprofloxacin	85	9.4
Colistine	85	0
Gentamycine	85	1.2
Nalidixic acid	85	5.9
Sulphametoxasol	85	27.1
Tetracycline	85	34.1
Tigeciklin	85	0
Trimethoprim	85	4.7

Antimicrobial resistance of indicator bacteria *E. coli* isolated from coecal samples of calves under 1 year in 2015. godine- EU / cyprofloxacin

RESULTS OF THE PRELIMINARY SURVEILLANCE IN AQUACULTURE

SENSITIVITY OF ISOLATED BACTERIA TO ANTIMICROBIAL SUBSTANCES

| Antimcrobial substance	OXYTETRA CYCLIN			POTENTIATED SULPHONAMID			FLUMEQIN			FLORFENICOL			ERYTHRO MYCIN		
BACTERIA	S*	I*	R*	S	I	R	S	I	R	S	I	R	S	I	R
Flavobacterium Psychrophilum n=40	36	4	2	23	15	2	40	0	0	40	0	0	0	0	40
Yersinia ruckeri n=30	22	5	3	26	4	0	28	2	0	30	0	0	0	0	30
Listonella anguillarum n=61	49	8	4	55	4	2	53	8	0	61	0	0	0	0	61
Tenacibaculum maritimum n=45	23	10	12	28	10	7	40	3	2	45	0	0	0	0	45

S* - sensitive
I* - intermediate
R* - resistent
ERYTHROMYCIN – antimicrobial used as negative control

AMR IN CROATIAN AQUACULTURE
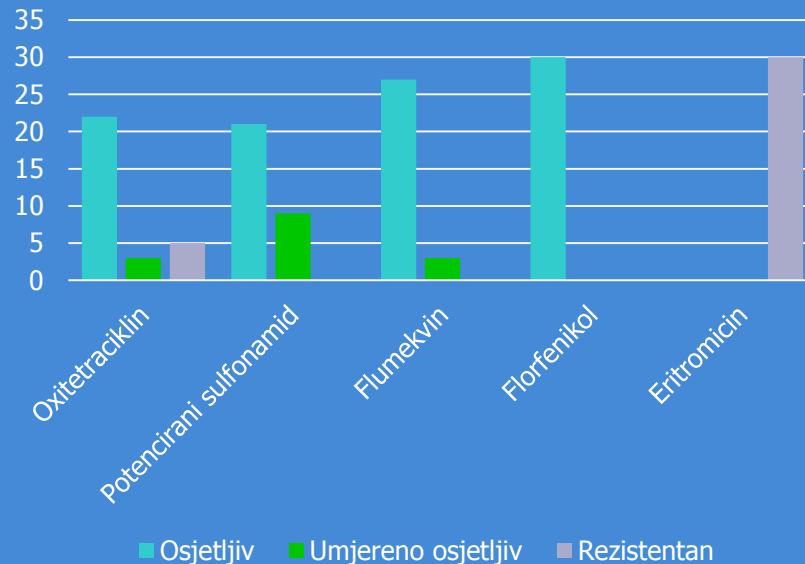
In freshwater fish in 2014.
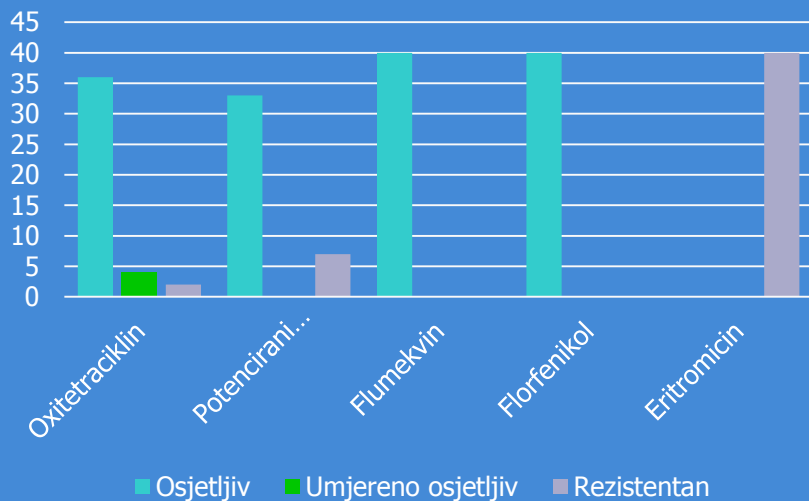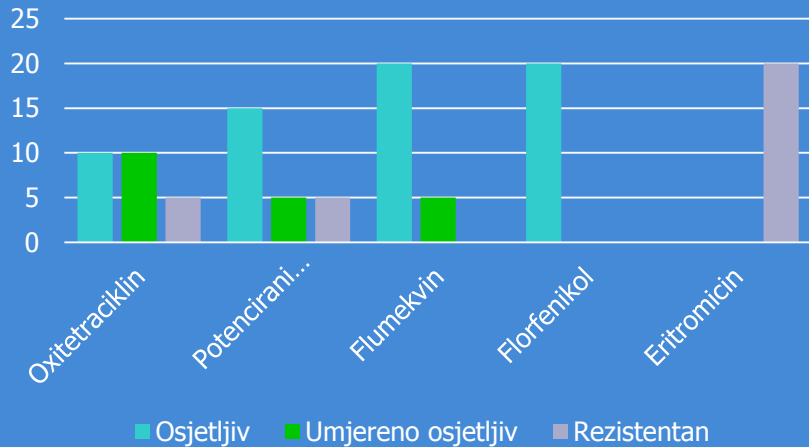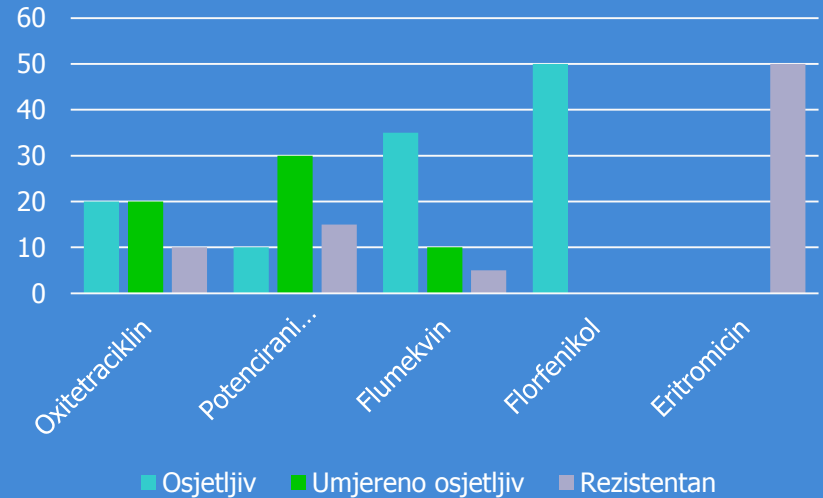
AMR IN AQUACULTURE

In marine aquaculture in 2014.

Listonella(Vibrio) anguillarum

Tenacibaculum maritimum

IF YOU HAVE COLD, VIRAL INFECTION, TAKE A REST, CURE YOURSELF BUT DO NOT USE THE ANTIBIOTICS WITHOUT DIAGNOSIS OF BACTERIAL PATHOGEN.

THANK YOU FOR YOUR ATTENTION