European Commission

Action Plan Against the rising threats from Antimicrobial Resistance: Road Map



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A. Appropriate use of antimicrobials Action n° 1: Strengthen the promotion of the appropriate use of antimicrobials in human medicines in all Member States. **Operational objectives Concrete activities** Milestones/Deadline Support the implementation of the Launch of the 2012-2014 preparatory action on Antimicrobial Resistance Final conference June 2016 provisions of the Council (grant from European Parliament) addressing Antimicrobial Resistance and Draft final report delivered Publication of final report expected mid-2017 Recommendation 2002/77/EC on causes of Non-prudent use of Antibiotics (ARNA)² project Misuse of antimicrobial agents in human medicine the prudent use of antimicrobial agents in human medicine¹ in Awareness across the whole chain of stakeholders: prescribers, Member States, notably regarding: pharmacists and patients. Prescription only requirements Sales of antimicrobial agents without a prescription Nursing homes and long term Consultation with MS on the implementation of Council Recommendation Report published mid-2016³ care facilities 2002/77/EC Education and training Through the Antibiotic Prescribing and Resistance in European Children Project completed mid-2014⁵ programmes (ARPEC)⁴ project 2010-2013 funded under Health Programme: development of web-based training providing educational modules on optimal antibiotic prescribing in children and antimicrobial resistance

¹http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=OJ:L:2002:034:TOC

²https://www.nivel.nl/en/arna

³http://ec.europa.eu/dgs/health_food-safety/amr/docs/amr_projects_3rd-report-councilrecprudent.pdf

⁴http://www.arpec.sgul.ac.uk/

⁵http://www.arpec.sgul.ac.uk/

Stimulate the appropriate use of antimicrobials in human	Development of EU Guidelines on Prudent Use of	Public Consultation of draft guidelines completed by ECDC 5
medicines	Antimicrobials in Human Medicine	September 2016
	Workshop "Best use of medicines legislation to bring new	Draft Guidelines reviewed by EU health security committee
	antibiotics to patients and combat the resistance problem",	10 November 2016
	prganised by EMA (8 November 2013, London)	
		Workshop conclusions published (December 2013) ⁸
	Ongoing activities on the modernisation of SmPC of "old	
	antibiotics" and harmonisation of the product information	
	across EU - referrals article 30/31 of Directive 2001/83/EC	
	through scientific evaluation that is performed by EMA CHMP	
	and with input from EC funded projects AIDA ⁶ and	
	MagicBullet ⁷	
Research on improving the appropriate use of antimicrobials	The project "Genomics to combat Resistance against	Publication in The Lancet Infectious Diseases (February
	Antibiotics in Community acquired low respiratory tract	2013) ¹⁰
	infections in Europe" (GRACE) ⁹ funded under the EU	,
	Framework Programme for Research demonstrated that	
	antibiotics should not be generally prescribed to patients with	
	uncomplicated lower respiratory tract infections (non-	
	pneumonic infections).	
	The EU Framework Programme for Research funded project	Book published in 2015 ¹²
	The appropriateness of prescribing antibiotics in primary	Articles published in BMC Family Practice (2014) ¹³ and PLoS
		One (2015) ¹⁴
	(APRES) ¹¹ assesses the appropriateness of prescribing	
	antibiotics in primary care in 9 European countries.	
	principal countries.	

⁶http://www.aida-project.eu/ ⁷http://cordis.europa.eu/result/rcn/140198_en.html

⁷ http://cordis.europa.eu/result/rcn/140198_en.html ⁸ http://www.ena.europa.eu/docs/en_GB/document_library/Report/2013/12/WC500158230.pdf ⁹ http://www.2020-horizon.com/GRACE-Genomics-to-combat-resistance-against-antibiotics-in-community-acquired-LRTI-in-Europe(GRACE)-s28368.html ¹⁰ https://www.nobi.nlm.nih.gov/pubmed/23265995 ¹¹ https://www.nivel.nl/en/apres ¹² http://www.nivel.nl/en/node/2430?database=ChoicePublicat&priref=1002669 ¹³ http://www.nivel.nl/en/node/2430?database=ChoicePublicat&priref=4959 ¹⁴ http://www.nivel.nl/en/node/2430?database=ChoicePublicat&priref=5653

Action n° 2:			
Strengthen the regulatory framework on veterinary medicines and on medicated feed.			
Operational objectives	Concrete activities	Milestones / Deadline	
To address Antimicrobial Resistance related to the use of veterinary medicinal products		Veterinary Medicines legislation: Commission proposal adopted in 2014 and sent to the EP and the Council. Negotiations between the institutions should take place at least until mid-2017.	
	Revision of the Medicated Feed Legislation ¹⁶ Set harmonised limits for residues for veterinary medicines in non-target animal feed related to the production of medicated feed, ban the preventive use of antibiotics via medicated feed and tighten the rules to prescribe and use medicated feed with antimicrobials.	Medicated Feed legislation: Commission proposal adopted in 2014 and sent to the EP and the Council. Negotiations between the institutions should take place at least until mid-2017.	
To verify on-the-spot that Member States meet all of their obligations with respect to the existing and revised regulatory framework on veterinary medicines and medicated feedstuffs.	the second half of 2015 and, carry out a series of fact-finding missions in selected Member States in 2016. This DG SANTE Directorate F project will generate an overview report.	All Member States, Iceland, Norway, Switzerland and stakeholders (Advisory Group on the Food Chain and Animal and Plant Health members and FVE member organisations) received the questionnaire in August 2015. Nine fact-finding missions in Member States to be completed during 2016; with an interim overview report to be drafted by the first quarter of 2017 and published. It has been decided to extend the project and a further seven fact-finding missions are planned for 2017 with a final overview report to be prepared during 2018 and published. Available mission reports are published on the DG SANTE website. ¹⁷	

¹⁵http://ec.europa.eu/health/veterinary-use/rev_frame_index_en.htm
¹⁶http://ec.europa.eu/food/safety/animal-feed/medicated-feed/index_en.htm
¹⁷http://ec.europa.eu/food/audits-analysis/audit_reports/index.cfm

Action n° 3:

Introduce recommendations for prudent use in veterinary medicine, including follow-up reports.

Operational objectives	Concrete activities	Milestones / Deadline
Use existing legal tools to the utmost to ensure prudent use of antimicrobials in the	Commission decision on referral in relation to 3rd and 4th generation cephalosporins	Adopted on 13 January 2012 ¹⁸
veterinary sector	Scientific recommendations of the EMA Antimicrobial Advice Ad Hoc Expert Group (AMEG) endorsed by the Committee for Medicinal Products for Veterinary Use (CVMP) and the Committee for Medicinal Products for Human Use (CHMP) on the need for further referrals of critically important antimicrobials that are already authorised for use in veterinary medicine and are considered as critically important for humans	Published July 2013 ¹⁹
	To initiate referrals on veterinary medicinal products taking into account the updated priority list for referrals as established by European Medicines Agency (EMA)	Referral on products containing colistin as a sole active substance of oral administration in food producing animals was initiated in 2014. The CVMP final opinion resulted in a Decision by the European Commission on 16 March 2015. ²⁰
		Referral on all veterinary medicinal products containing colistin in combination with other antimicrobial substances for oral administration was initiated in May 2015. The CVMP final opinion resulted in a Decision by the European Commission on 14 July 2016. ²¹
	CVMP-reflection paper of November 2011 on the use of macrolides, lincosamides and streptogramins	Published in June 2013 ²²
	Request to EFSA for a Scientific Opinion on the Risk for the development of Antimicrobial Resistance (AMR) due to feeding of calves with milk containing residues of antibiotics ²³	EFSA scientific opinion expected to be completed in December 2016 and published in January 2017

http://ec.europa.eu/health/documents/community-register/2012/20120113113370/dec_113370_en.pdf

- ¹⁹http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000639.jsp& ²⁰Official Journal of the European Union, C 148, 5.5.2015
- http://ec.europa.eu/health/documents/community-register/2015/20150316130649/dec_130649_en.pdf http://ec.europa.eu/health/documents/community-register/2015/20150316130649/anx_130649_en.pdf ²¹Official Journal of the European Union, C 312, 26.8.2016,

¹⁸C(2012)182

http://ec.europa.eu/health/documents/community-register/2016/20160714135332/dec_135332_en.pdf http://ec.europa.eu/health/documents/community-register/2016/20160714135332/anx_135332_en.pdf

²²http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2011/11/WC500118230.pdf

²³http://registerofquestions.efsa.europa.eu/roqFrontend/questionLoader?question=EFSA-Q-2015-00611

To have scientific recommendations on the		Final advice published in 2013 and in 2014 ²⁵
use in the veterinary sector of last resort	726/2004) of Agency Committee for Medicinal Products for Veterinary	See also Action 7
antimicrobials for humans (e.g. tigecycline	Use (CVMP) and the Committee for Medicinal Products for Human	
and colistin)	Use (CHMP) on the use of last resort antimicrobials in the veterinary	Updated advice on colistin use in animals published on 27
		July 2016 ²⁶
	CVMP reflection paper on the risk of antimicrobial resistance transfer	Published in 30 January 2015 ²⁷
	from companion animals	
	CVMP reflection paper on the use of pleuromutilins in food-producing	Published on February 2014 ²⁸
	animals in the European Union	
	CVMP draft guideline on the assessment of the risk to public health	Published on March 2015 ²⁹
	from antimicrobial resistance due to the use of an antimicrobial	
	veterinary medicinal product in food-producing animals	
		Published on 6 October 2016 ³⁰
	8) 8)	A workshop took place on 26 November 2015 with
	prepared by the Antimicrobial Advice Ad Hoc Expert Group (AMEG) ³¹	Member States and stakeholders in order to determine
		whether there is a need for a follow-up of this advice and if
		so, the type of activities that could be elaborated ³²
		EFSA and EMA joint scientific opinion expected to be
		completed in December 2016 and published in January
		2017
	(RONAFA, reduce overall need of use of antimicrobials), which	2011
	included a specific request to assess the recent scientific	
	developments in the areas of possible alternatives to the use of	
	antimicrobials in animal husbandry in the EU ³³	
To reduce the overall use of antimicrobials in		Commission Guidelines for the prudent use of
veterinary medicine (better targeted		antimicrobials in veterinary medicine were published in September 2015 ³⁴
treatments, use according to best practices,		
etc)	developing national strategies on prudent use.	han han an tation, but the Manakan Otatao is hair. (1997)
		Implementation by the Member States is being followed-
		up by SANTE Directorate F during fact-finding missions on
		the prudent use of antimicrobials in animals in 2016 and
		2017.

²⁴ http://www.ema.europa.eu/docs/en_GB/document_library/Other/2013/04/WC500142070.pdf
²⁵ http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000639.jsp&mid=WC0b01ac058080a585
²⁶ http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2016/07/WC500211080.pdf

²⁷http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_001485.jsp&mid=WC0b01ac0580a74c89

²⁸http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_001486.jsp&mid=WC0b01ac0580a74c89
²⁹http://www.ema.europa.eu/ema/index.jsp?curl=pages/home/general/general_content_001483.jsp&mid=WC0b01ac0580a74c89
³⁰http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2016/10/WC500214901.pdf

³¹http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000639.jsp&mid=WC0b01ac058080a585

³²http://ec.europa.eu/dgs/health_food-safety/amr/events/ev_20151126_en.htm

³³http://registerofquestions.efsa.europa.eu/roqFrontend/questionLoader?question=EFSA-Q-2015-00216

³⁴http://ec.europa.eu/health/antimicrobial_resistance/docs/2015_prudent_use_guidelines_en.pdf

Guarantee responsible and efficient use of medicated feed	Raising awareness of the control authorities to risks due to different routes of oral administration of antimicrobials in order to detect misuse and to take remedial action	Current and follow-on to Action 2
To verify on-the-spot that the Member States have acted upon whatever Commission recommendations are proposed for the prudent use of antimicrobials in the Member States	Questionnaire sent in August 2015 and fact-finding missions in selected Member States during 2016- see DG SANTE Directorate F project undertaken pursuant to Action 2. How the Member States put the Commission's and/or national guidelines on prudent use into practice will be one of the elements of the DG SANTE Directorate F fact-finding missions.	All Member States, Iceland, Norway, Switzerland and stakeholders (Advisory Group on the Food Chain and Animal and Plant Health members and FVE member organisations) received the questionnaire in August 2015. Nine fact-finding missions in Member States to be completed during 2016; with an interim overview report to be drafted by the first quarter of 2017 and published. It has been decided to extend the project and a further seven fact-finding missions are planned for 2017with a final overview report to be prepared during 2018 and published. Available mission reports are published on the DG SANTE website. ³⁵
In the course of evaluating Member States residue monitoring plans, focus on the ability of the national laboratories to effectively monitor for residues of antimicrobials of concern (critically important antimicrobials including fluoroquinolones, 3 rd and 4 th generation cephalosporins and macrolides).	methodology by the EU Reference Laboratory for antimicrobial residues.	The evaluation of the 2013 residues monitoring plans was completed in November 2013 and the EURL assessment was provided in February 2014. DG SANTE Directorate F overview report has been finalised and published and presented to Member States and EU agencies at the AMR working group meeting of 1 July 2015. ³⁶

³⁵http://ec.europa.eu/food/audits-analysis/audit_reports/index.cfm
³⁶http://ec.europa.eu/food/audits-analysis/overview_reports/details.cfm?rep_id=77

B. Prevent microbial infections and their spread Action n° 4: Strengthen infection prevention and control in healthcare settings. **Operational objectives Concrete activities Milestones / Deadline** Adopted and published November 2012³⁸ Monitor and support the st Report of the Commission on the implementation of the Council implementation of the Council Recommendation on patient safety, including healthcare associated Recommendation on patient safety infections. incl. healthcare associated infections 2nd Report of the Commission on the implementation of the Council Adopted and published June 2014^{3s} (HAI)³⁷ with emphasis on: Recommendation on patient safety, including healthcare associated Development of guidance on infections. infection prevention and control Support via the Health Programme projects/actions to follow up the priority Joint Action on Antimicrobial Resistance and Healthcare-Strengthened surveillance of HAI areas on which future work should focus include, as identified in the Associated Infection Included in 2016 EU Health Education and training of Commission's implementation report Programme Workplan. The Joint Action is expected to be launched in spring 2017 healthcare workers Several guidance documents published by ECDC^{40,47} Information to patients Continue fostering with the European Centre for Disease Prevention and Control (ECDC) the development of guidance on infection prevention and control, strengthening healthcare-associated infections (HAI) surveillance and Directory of online resources for prevention and control of AMR and HAI published on ECDC website⁴² the development of training curricula for healthcare workers. Several reports and protocols on HAI surveillance published by ECDC^{43,44} Core competencies for infection control and hospital hygiene professionals in the EU, and other training resources published by ECDC⁴⁵

³⁷http://ec.europa.eu/health/patient_safety/docs/council_2009_en.pdf

³⁸http://ec.europa.eu/health/patient_safety/docs/council_2009_report_en.pdf

³⁹http://ec.europa.eu/health/patient_safety/docs/ec_2ndreport_ps_implementation_en.pdf

⁴⁰http://ecdc.europa.eu/en/healthtopics/Healthcare-associated_infections/guidance-infection-prevention-control/Pages/guidance-organisation-infection-prevention-control.aspx

⁴¹http://ecdc.europa.eu/en/healthtopics/Healthcare-associated_infections/guidance-infection-prevention-control/Pages/guidance-prevention-control-infections-CRE.aspx

⁴²http://ecdc.europa.eu/en/healthtopics/healthcare-associated_infections/guidance-infection-prevention-control/pages/guidance-prevention-control-infections-caused-by-multidrug-resistant-bacteria-and-healthcare-associated_infections.aspx

⁴³http://ecdc.europa.eu/en/healthtopics/Healthcare-associated_infections/surgical-site-infections/Pages/SSI.aspx

⁴⁴http://ecdc.europa.eu/en/healthtopics/Healthcare-associated_infections/Clostridium-difficile-infections/Pages/Clostridium-difficile-infections.aspx

⁴⁵http://ecdc.europa.eu/en/healthtopics/Healthcare-associated_infections/training-infection-control/Pages/training.aspx

Action n° 5:

Adoption of a proposal for an EU Animal Health Law.

Operational objectives	Concrete activities	Milestones / Deadline
To create an animal health legal framework based on the principle "prevention is better than cure".	 animal health and biosecurity; clarify the responsibility of veterinary and aquatic animal health professionals to adopt effective measures to prevent the spread of pathogens and to raise awareness; clarify responsibility of competent authorities to protect animal health, human health and the environment through reduction of the risks arising from the emergence, introduction or spread of pathogens; 	The final rule was published on 31 March 2016 as Regulation (EU) 2016/429 of the European Parliament and of the Council of 9 March on transmissible animal diseases and amending and repealing certain acts in the area of animal health ("Animal Health Law"). ⁴⁶ It already entered into force and most of its provisions will be applicable as from 21 April 2021.Further details are foreseen in subsequent delegated and implementing acts as appropriate, some of these are to be laid down by 21 April 2019, others by undefined later dates.

 $^{^{46}} http://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1476967773427 \& uri=CELEX:32016R0429$

C. Develop new effective antimicrobials or alternatives for treatment

Action n° 6:

To promote, in a staged approach, unprecedented collaborative research and development efforts to bring new antibiotics to patients.

Operational objectives	Concrete activities	Milestones / Deadline
To re-activate research and development by industry for new antibiotics and related issues	Calls for proposals via the Innovative Medicine Initiative (IMI), a public- private partnership between the Commission and the industry. IMI ⁴⁷ projects are funded by the Commission, via Framework Programme 7and Horizon 2020, and the European Federation of Pharmaceutical Industries and Associations.	2014 and will run for 10 years. Its goal is to develop next generation vaccines, medicines and treatments, such as new antibiotics. It will build on the successes and lessons learnt under IMI 1. It will tackle Europe's growing health challenges, and secure the future international competitiveness of Europe's pharmaceutical industry.
	To support the development of rapid point-of-care tests for appropriate use of antibiotics.	The project RAPP-ID started in April 2011 for a duration of 60 months ⁴⁸
	 The launch of a large IMI programme "New Drugs 4 Bad Bugs"⁴⁹ that aims to bring new antibiotics to patients and currently covers: 1) innovative trial design and clinical drug development 2) learning from success and failure and getting drugs into bad bugs, and 3) discovery and development of new drugs for combating Gram-negative infections 4) Driving re-investment in R&D and responsible use of antibiotics 5) Clinical development of antibacterial agents for Gram-negative antibiotic resistant pathogens 6) Systemic molecules against health care associated infections 7) Inhaled anti-bacterials in bronchiectasis and cystic fibrosis This programme has a budget of more than € 600 million. 	Two IMI Projects of the 6 th call were launched in February 2013. COMBACTE ⁵⁰ pioneers new ways of designing and implementing efficient clinical trials for novel antibiotics and TRANSLOCATION ⁵¹ aims to increase the overall understanding of how to get antibiotics into multi-resistant Gram-negative bacteria. Project ENABLE ⁵² puts in place an antibiotic drug development platform. The project aims to advance the most promising early discovery stage of novel antibiotic molecules from the academic and SME sector to early clinical development. ND4BB project DRIVE-AB ⁵³ , launched October 2014, will develop concrete recommendations for new commercial models that provide industry with an incentive to invest in antibiotic development while ensuring that new antibiotics are used wisely.

- ⁴⁷http://www.imi.europa.eu/
 ⁴⁸http://www.imi.europa.eu/content/rapp-id
 ⁴⁹http://www.imi.europa.eu/content/nd4bb
 ⁵⁰https://www.imi.europa.eu/content/combacte-net
 ⁵¹http://www.imi.europa.eu/content/translocation
 ⁵²http://www.imi.europa.eu/content/enable
 ⁵³https://www.imi.europa.eu/content/drive-ab

		In February 2015, COMBACTE-MAGNET ⁵⁴ was launched which aims to bring highly innovative studies and activities related to prevention and treatment of infections caused by multi-drug resistant Gram-negative bacteria. Project COMBACTE-CARE ⁵⁵ launched in March 2015 aims to shed new light on the best ways to understand and treat Carbapenem resistant infections. The latest project, iABC ⁵⁶ , started in August 2015 and will develop two inhaled antibiotics to help cystic fibrosis and bronchiectasis patients.
To assess the possibilities for	To launch a dialogue with the health authorities of the Member States and	IMI-2 launched its 9th Call in April 2016 addressing the clinical burden of Clostridium difficile infection (CDI). ⁵⁷ Event on the best use of medicines legislation to bring
increasing the efficiency of the market authorisation process in	other relevant stakeholders in view of a co-ordinated approach to introduce incentives for the development and marketing of new antibiotics.	new antibiotics to patients and combat the resistance problem (8 November 2013)
relation to new antibiotics		EMA workshop on the use of pharmacokinetics and pharmacodynamics in the development of antibacterial medicinal products (12-13 November 2015)
	effect - 1 February 2017).	Ongoing discussions with EMA & STAMP expert group on optimisation of existing regulatory tools for all medicines, including antibiotics
	In March 2016, the EMA launched a new scheme "PRIME" to enhance support for the development of new innovative medicines that target an unmet medical need. The PRIME has the potential to encourage the development and accelerate approval of a new class of antibiotics.	
	In light of the results of the assessment mentioned above, to identify possibilities of simplification/streamlining of testing/assessment requirements/procedures and accelerating the assessment process for new antimicrobials and where relevant launch a revision of the relevant guidelines	
Discussion with international partners identifying areas of potential cooperation		In September 2016, the EMA hosted a two day meeting between three regulatory agencies EMA, Pharmaceuticals and Medical Devices Agency in Japan (PMD) and Food and Drug Administration in the USA (FDA) on Antibacterial Drug Development. The outcome of the meeting was presented at the G7 Kobe Health Ministers' Meeting.

⁵⁴http://www.imi.europa.eu/content/combacte-magnet
 ⁵⁵http://www.imi.europa.eu/content/combacte-care
 ⁵⁶https://www.imi.europa.eu/content/iabc
 ⁵⁷http://www.imi.europa.eu/content/imi-2-call-9

Action n° 7:

Promote efforts to analyse the need for new antibiotics into veterinary medicine.

Operational objectives	Concrete activities	Milestones / Deadline
To analyse the need for new antibiotics into veterinary medicine		Final advice published in 2014 ⁵⁸ See also Action 3
		A workshop took place on 26 November 2015 with Member States and stakeholders in order to determine whether there is a need for a follow-up of this advice, and if so, the type of activities that could be elaborated. ⁶⁰
To facilitate the use of alternatives that may reduce the need for		Authorisation of additives is dependent on applications received
treatment with antimicrobials	the need to use antimicrobial agents in animal husbandry in the European	EFSA and EMA joint scientific opinion expected to be completed in December 2016 and published in January 2017

 ⁵⁸http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000639.jsp&mid=WC0b01ac058080a585
 ⁵⁹http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000639.jsp&mid=WC0b01ac058080a585
 ⁶⁰http://ec.europa.eu/dgs/health_food-safety/amr/events/ev_20151126_en.htm
 ⁶¹http://registerofquestions.efsa.europa.eu/roqFrontend/questionLoader?question=EFSA-Q-2015-00216

D. Joining forces with international partners to contain the risks of spreading AMR from international trade and travel and via the environment

Action n° 8:

Develop and/or strengthen multilateral and bilateral commitments for the prevention and control of AMR in all sectors.

Operational objectives	Concrete activities	Milestones / Deadline
Maintain and deepen EU/US transatlantic cooperation addressing		TATFAR progress report published May 2014 ⁶³
AMR	(TATFAR) Recommendations ⁶²	Face-to-face meeting during of TATFAR group took place
	Bi-annual TATFAR audio-conference meetings and organisation of a face-to-	on 22-23/10/2015 as an associated event of the
	face meeting with part of the group to review progress and discuss follow-up	Luxembourgish Presidency and it was decided to prolong
		TATFAR (2016-2020). TATFAR Work plan for 2016-2020
		adopted 1 st quarter 2016. TATFAR expanded to include
	2016). The taskforce decided to continue with 15 recommendations, retiring	Canada and Norway from October 2016.
	two, and created one new recommendation on knowledge gaps regarding the transmission to human of antimicrobial resistance arising out of use of	TATEAD sublication on new business models for
		TATFAR publication on new business models for antimicrobial development ⁶⁴ (accepted manuscript) and on
		knowledge gaps regarding the transmission to human of
		antimicrobial resistance arising out of use of antimicrobials
		in animals (June 2016) 65 .
Discussion with international		2016 Joint Action on Antimicrobial Resistance and
partners identifying areas of		Healthcare-Associated Infection under development with
cooperation		EU Member States, Norway, Serbia and Moldova to
		include activities on evaluation of 'one health national
		action plans', prudent use of antimicrobials, awareness
		raising. The Joint Action is expected to be launched in
		spring 2017, see also Action 4.
		1st Seminar China-EU (Beijing) March 2013
		2nd Seminar China-EU (first half 2015)
		Comparative studies on policies (ongoing) AMR as standing item of meetings of the Russian
		Federation Sub-group on Communicable Diseases (on
		hold)
		Commission and EEAS holding conference on AMR in
	Colombia, Paraguay, Peru and Uruguay)	Rio, Brazil January 2017, followed by 6 seminars on
		different AMR topics in partner country capitals over 2017
		and 2018.

⁶²http://ecdc.europa.eu/en/activities/diseaseprogrammes/TATFAR/Documents/210911_TATFAR_Report.pdf

⁶³http://cdd.edu/area/disease/pdg/anmes/14717402004mend/2 ⁶³http://www.cdc.gov/drugresistance/pdf/tatfar-progress_report_2014.pdf ⁶⁴http://cid.oxfordjournals.org/content/early/2016/08/29/cid.ciw593.full.pdf+html

⁶⁵ http://www.cdc.gov/drugresistance/pdf/tatfar-report---recommendation-18.pdf

United Nations	Cooperation with international partners in UN, WHO, OIE and FAO to raise awareness on AMR and gain political commitment globally to implement the WHO Global Action Plan	Political Declaration and participation in UN high-level meeting on AMR at United Nations General Assembly September 2016
World Health Organization (WHO)	 Cooperation with WHO to support development of WHO Global Action Plan Grant to WHO to implement the pilot project on mapping the global threat of AMR in sub Saharan Africa – 750 000 EUR 	 Participation to WHO meetings related to the development of the WHO Global Action Plan Provide input to WHO consultation on global action plan Grant contract with WHO to be signed 1st semester 2017; work to be carried out 2017-2018
Implementation of the World Health Organization (WHO/Europe)-DG Health and Food Safety "Health	Annual WHO/Europe / EC Senior officials meetings reviewing WHO/Europe- DG Health and Food Safety "Health Security Roadmap"	WHO-EC meeting May 2013 WHO-EC meeting June 2014 WHO-EC meeting February 2015
Health and Food Safety "Health Security Roadmap" identifying Antimicrobial Resistance as an area for cooperation"	Cooperation to support capacity building (laboratories in charge of surveillance of AMR in the food chain) in non EU Member States	Several workshops and trainings (2014-2015)
World Organisation for Animal Health (OIE)	Support to the Conference on Antimicrobial Resistance organized by the World Organisation for Animal Health (OIE)	March 2013
	Collaboration revision chapters on AMR of the Terrestrial and Aquatic Codes and participation on ad hoc groups AMR	August 2013, January- July-December 2014
OECD	Grant to OECD on economic burden of AMR Two year action to assess the health and economic burden of AMR and produce a model to assess policy impacts.	2016 grant to OECD agreed under the EU Third Health Programme
European Observatory	Grant to European Observatory Mapping and analysis of good practices and a book of evidence on good practices and enablers / obstacles to their transfer.	2016-2017 grant to European Observatory agreed under the EU Third Health Programme
Food and Agricultural Organization (FAO)	Bilateral meeting FAO-EC	September 2014
To identify options for addressing potential risks from pharmaceuticals in the environment	Development of a strategic approach to pharmaceuticals in the environment	Outcome expected in 2017

Rationale use of medicines through the Renewed Partnership (2012- 2016) EU-WHO in 15 countries ⁶⁶	 Provide technical assistance to countries to update their list of essential medicines, their Standard Treatment Guidelines and their National Formulary 	Depends on the countries (x15)- below some examples: a) Burundi: Training of trainers on the use of guidelines
2016) EU-WHO IN 15 countries	 Provide technical assistance to countries to survey prescribing, dispensing and use of medicines using WHO methodology- Done in Ghana Provide technical assistance to countries for improving prescribing, dispensing and use of medicines in public sector facilities- Tanzania: dispensers and prescribers from 10 districts trained in rational medicine 	 for medicinal products in health centers b) DRC: Perform a survey of prescribing practices, dispensing and use of antibiotics in the Eastern Region.
comprehensive support to national policy and plans Global Health Security Agenda	Health is a sector of concentration in 17 countries. ⁶⁷ The main approach is to provide a comprehensive and coordinated support to the developing countries. Pharmaceutical strategic plans would cover aspects of medicines regulation, public sector procurement, supply and distribution and medicines use. Cooperating and steering international activities with forum of countries active on AMR	On-going with the development of the activities under the 11 [™] European Development Fund (EFD) GHSA meeting on international surveillance May 2016

⁶⁶Burundi ; Cameroon ; Congo ; DRC ; Ethiopia ; Ghana ; Guinea-Conakry ; Kenya ; Mali ; Mozambique ; Senegal ; Tanzania ; Togo ; Zambia ; Zimbabwe. ⁶⁷Burkina Faso ; Guinea-Conakry ; Guinea Bissau ; Mauritania ; Nigeria ; Burundi ; CAR ; DRC ; Ethiopia ; South-Soudan ; Zimbabwe ; Afghanistan ; Tajikistan ; Morocco and Grenada.

E. Monitoring and surveillance		
Action n° 9:		
Strengthen surveillance systems	on AMR and antimicrobial consumption in human medicine.	
Operational objectives	Concrete activities	Milestones / Deadline
Strengthen surveillance systems on antimicrobial resistance and antimicrobial consumptions	Ensuring the sustainability of the European Surveillance system of Antimicrobial Consumption (ESAC). Transfer of the European Surveillance system of Antimicrobial Consumption to the European Centre for Disease Prevention and Control (ECDC).	Completed December 2012. The system adopted the name of "European Surveillance of Antimicrobial Consumption Network" (ESAC-Net)
		Several EARS-Net and ESAC-Net reports published by ECDC, together with summaries of data and updates of interactive databases ⁶⁸ : November each year Several reports on point prevalence surveys published by ECDC: acute care hospitals, July 2013 ⁶⁹ ; long-term care facilities, May 2014. ⁷⁰ Two additional European point prevalence surveys, in acute care hospitals and in long-term care facilities are currently coordinated by ECDC (2016-2017).
	Implementation of the newly adopted measures on new case definitions for antimicrobial resistance and healthcare-associated infections (Commission Implementing Decisions 2012/506/EU of August 2012 under Decision No 2119/98/EC of the European Parliament and of the Council) ⁷¹	Decision adopted 2012. Monitor of the implementation: by December 2015. Review of the Decision in progress as part of the updating of legislation following adoption of Decision 1082/2013 on serious cross border threats to health.
	Addressing the lack of data on antimicrobial resistance and antimicrobial consumption in children: Completion of the Antibiotic Prescribing and resistance in European Children (ARPEC) project ⁷²	Completed 2014

⁷⁰/₆₈http://ecdc.europa.eu/en/healthtopics/antimicrobial-resistance-and-consumption/Pages/antimicrobial-resistance-and-anitmicrobial-consumption.aspx
⁶⁹/₆₉http://ecdc.europa.eu/en/healthtopics/Healthcare-associated_infections/point-prevalence-survey/Pages/Point-prevalence-survey.aspx
⁷⁰/₇₀http://ecdc.europa.eu/en/healthtopics/Healthcare-associated_infections/point-prevalence-survey-long-term-care/Pages/point-prevalence-survey-long-term-care-facilities.aspx
⁷¹/₇₁http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2012:262:0001:0057:EN:PDF
⁷²/₇₂http://www.arpec.sgul.ac.uk/

Action n° 10:			
Strengthen surveillance systems on AMR and antimicrobial consumption in animal medicine.			
Operational objectives	Concrete activities	Milestones / Deadline	
and monitoring on the occurrence of antimicrobial resistance and consumption of antimicrobials will provided the necessary data on the use of antimicrobials and on the impact of antimicrobial consumption on the occurrence of antimicrobial resistance in the food chain (animals and food) in the EU.	 European Surveillance of Veterinary Antimicrobial Consumption (ESVAC)⁷³ project coordinated by the European Medicines Agency on collection data on the consumption of antimicrobials on a multiphase approach: Pilot project collecting standardized overall sales data Collecting and report overall national sales data from all Member States 	 6th ESVAC report was published in October 2016 - on sales in 2014 (26 Member States, 2 EEA countries and Switzerland provided data. Pilot project on collection data per species was initiated in 2014. After the test phase, the project was postponed due to insufficient number of participating countries. Meanwhile, data collection protocols for the project are being developed. Commission proposal for review of veterinary medicines 	
	for veterinary medicines	legislation, adopted in 2014 (see Action 2) provides for compulsory collection of data on sales and use.	
	Harmonization of surveillance and monitoring of antimicrobial resistance in the food chain:		
	Request of scientific and technical assistance to the European Food Safety Authority (EFSA) on harmonizing monitoring in bacteria transmitted through food	EFSA opinion on harmonization monitoring AMR published in 2012 ⁷⁴	
	New legal framework for harmonised monitoring of antimicrobial resistance in zoonotic and commensal bacteria in the food chain	Decision 2013/652/EU ⁷⁵ on harmonised monitoring and reporting of antimicrobial resistance in the food chain in the EU	
	Financial contribution from the Union to the harmonized monitoring of AMR carried out by the Member States	Decision 2013/653/EU ⁷⁶ financial aid towards a coordinated control plan for AMR monitoring in 2014. Financial aid for 2015: individual grant decision sent to the Member States in February 2015.	
	Request of scientific and technical assistance to the European Food Safety Authority (EFSA) on randomisation of sampling for the purpose of AMR monitoring	EFSA opinion on randomisation of sampling for monitoring AMR published in May 2014 ⁷⁷	

 ⁷³http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000302.jsp
 ⁷⁴http://www.efsa.europa.eu/en/efsajournal/pub/2742 and http://www.efsa.europa.eu/en/efsajournal/pub/2897
 ⁷⁵http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32013D0652
 ⁷⁶http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32013D0653
 ⁷⁷https://www.efsa.europa.eu/en/efsajournal/pub/3686

Surveillance and monitoring of the occurrence of pathogens in the framework of Animal Health Regulation. No treatment of animals without proper diagnosis; in particular treatment should not jeopardize detection of certain maior pathogens.		The same as for Action 5, see update there, including also the link to the official text and full details of the final rule as adopted by the European Parliament and Council.
monitoring of AMR. Identify good practices. Gather information on voluntary monitoring systems.	Preparation of a final overview report (evaluation of the implementation of Decision 2013/652/EU by Member States, identification of common difficulties and good practices).	Two pilot audits were carried out in the autumn of 2015. Six audits in Member States to be completed by the end of 2016. For 2017 seven further audits are planned in six Member States and Switzerland. Reports are published on DG SANTE website. ⁷⁸ Interim overview report to be prepared by March 2017 and published and a final overview report to be prepared by the end of the first quarter of 2018 and also published.
consumption collected by the three	Request from the Commission to the 3 Agencies (EFSA, EMA and ECDC) on the establishment of a new organisational structure to improve the analysis of the data on AMR and consumption (Joint Interagency Antimicrobial Consumption and Resistance Analysis Report, JIACRA). Follow-up of the scientific Joint Interagency Antimicrobial Consumption and	
		The second JIACRA report is to be published by June 2017
	Request for a joint ECDC, EFSA and EMA scientific opinion on a list of outcome indicators as regards surveillance of antimicrobial resistance and antimicrobial consumption in humans and food-producing animals	The Joint ECDC, EFSA and EMA Scientific Opinion is expected by September 2017

⁷⁸http://ec.europa.eu/food/audits-analysis/audit_reports/index.cfm
⁷⁹http://www.efsa.europa.eu/en/efsajournal/pub/4006

F. Additional Research and Innovation Action n° 11: Reinforce and co-ordinate research efforts. **Milestones / Deadline Operational objectives Concrete activities** An overview of EU supported research activities was Reinforce antimicrobial resistance An overview of research projects related to drug resistance can be found at: research in a coordinated fashion in http://ec.europa.eu/research/health/index.cfm?pg=area&areaname=amdr published in The Lancet in August 2016⁸⁰ three different thematic areas within the last calls of the seventh Framework Programme for Research Under the 7th Framework Programme the European Commission has 2007 -2013 published Research Work Programmes in which call topics on AMR were published in a coordinated manner: HEALTH Work Programme (WP) (https://ec.europa.eu/research/participants/portal/doc/call/fp7/common/15676 45-1. health upd 2013 wp 27 june 2013 en.pdf) Knowledge Based Bio-Economy (KBBE) Work Programme http://ec.europa.eu/research/participants/data/ref/fp7/132093/b-wp-201301 en.pdf) and the Nanotechnologies, Advanced Materials and. Production (NMP) Work programme (http://ec.europa.eu/research/participants/data/ref/fp7/132117/d-wp-201301 en.pdf) The codes below refer to the call topics in the Work Programmes: WP2013, call7, topic KBBE.2013.1.3-05 for €9 Mio EU contribution Project EFFORT⁸¹, which studies the ecology and Antimicrobial transfer throughout the WP2013, call 7, KBBE topics KBBE.2013.1.1-01, KBBE.2013.1.3-03, food chain transmission of AMR from farm to fork, started in KBBE.2013.3.5-01 for a total of €21Mio EU contribution December 2013. WP2012, call6, topics KBBE.2012.1.2-10 & KBBE.2012.1.4-04; Antimicrobial resistance in farming Projects on Impact matrix analysis and cost-benefit and animal production calculations to improve management practices regarding health status in organic dairy farming ("IMPRO"⁸²) and on Targeted disease prophylaxis in European fish farming "TARGETFISH"⁸³) projects started 4th guarter 2012

⁸⁰http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(16)31425-8/fulltext

⁸¹http://www.effort-against-amr.eu/

⁸²http://www.dev.impro-dairy.eu/index.php/fr/

⁸³http://www.wageningenur.nl/en/show/TARGETFISH.htm

Dovelopment of diagnostic table for		
Development of diagnostic tools for infectious diseases	HEALTH.2012.2.3.0-1	Projects funded include: "Routine diagnostic tool for
Infectious diseases		urinary tract infections caused by extended spectrum beta
		lactamase and carbapenamase producing bacteria"
		(ROUTINE), "Rapid identification of respiratory tract
		infections (RID-RTI), "Development of a handheld
		antibacterial drug resistance diagnostic device using
		nanowire technology" (NANOMAL), "Automated next
		generation sequencing for diagnostic microbiology"
		(PATHSEEK), "Assured point-of-care device for
		Syphilis and HIV in pregnant women and new-born"
		(Preventit), "Rapid Aptamer based diagnostic for bacterial
		meningitis" (RAPTA Diag) and "Detection of persistent
		infections by human papillomaviruses" (PIPAVIR).
		More information is available on the CORDIS website. ⁸⁴
	PHC-12-2015 (SME Instrument)	Two projects are funded under the SME Instrument Phase
		II: Project "Respiratory- ImmunoDx" is about distinguishing
		bacterial versus viral lower respiratory tract infections at
		the PoC to facilitate the appropriate/targeted use of Abs.
		Project "PneumoSIP" aims to develop a fully automated
		PoC device for the fast quantitative aetiological diagnose
		of Community- Acquired Pneumonia (CAP) also analysing
		antibiotic resistances to enable appropriate treatment.
	HOA 8 - 2015: Horizon Prize	
		The EC launched on 26/2/2015 the Horizon Prize - Better
		use of Antibiotics, which offers a cash reward of €1 million
		to whoever who can develop a rapid test that will allow
		healthcare providers to distinguish, at the point of care,
		between patients with upper respiratory tract infections
		that require antibiotics and those that can be treated
		safely without them. ⁸⁵ Award decision: Q4 2016.

- ⁸⁴http://cordis.europa.eu/home_en.html
 ⁸⁵www.ec.europa.eu/horizonprize/antibiotics

Mobilise Small and medium	HEALTH.2013.2.3.1-1	Seven projects to support research and development of
enterprise (SME) to develop new		drugs, vaccines or alternative treatments for bacterial
antimicrobials and vaccines		infections have been funded. ⁸⁶ The work of 44 innovative
		SMEs is directly supported.
Research to the use of antimicrobial	sHEALTH.2013.2.3.1-2	Four funded projects seek to identify better methods to
via personalised approaches		use currently available antibiotics.
Developing novel nanotechnology	• NMP.2013.1.2-2	Four projects study the usage of novel nano technology
enabled therapies for bacterial infectious diseases	• HEALTH. 2012.2.3.1-1	for drug delivery.
Piloting personalised medicine in	SC1 PHC-24-2015	The "Personalised Risk assessment in febrile illness to
health and care systems		optimise Real-life Management across the European
		Union" (PERFORM) project will develop a comprehensive
		management plan for febrile children allowing
		discrimination of viral and bacterial infections. ⁸⁷
Support the Joint Programming		Participation in the Management Board of the JPI AMR as
Initiative (JPI) on Antimicrobial		a non-voting member and funding for the implementation
Resistance (AMR)		of this JPI via two coordination and support actions (since
		September 2012). The JPIAMR Strategic Research
		Agenda was launched 3 April 2014 ⁸⁸
	HCO 12 - 2015: ERA-NET	First H2020 WP published at the end of 2013 EC support
		of transnational research calls of JPIAMR via ERA-NET
		Co-fund scheme
		Information on the outcome of the closed calls is available
		on the JPIAMR website ⁸⁹
	1 st transnational call: InnovaResistance	
	• 2 nd transnational joint call on "transnational research on repurposing of	
	neglected antibiotics and characterizing antibiotics or antibiotic and non- antibiotic combinations to overcome bacterial antibiotic resistance".	
	• 3 rd transnational call: Transmission Dynamics – ERA-NET Cofund call	
	• 4 th transnational call: Research Networks Working Groups	

 ⁸⁶http://europa.eu/rapid/press-release_MEMO-13-996_en.htm
 ⁸⁷http://www.perform2020.eu/
 ⁸⁸http://www.jpiamr.eu/document-library/strategicresearchagenda/
 ⁸⁹http://www.jpiamr.eu/activities/open-call/

Contribute to a global mapping of drug resistance		Meeting between the World Health Organization (WHO) and the European Commission (EC) in January 2012,
	Cooperation and joint actions in the field of global mapping	participation in WHO Advisory Group 2013
Foster Innovation-Focus group on reduction of antimicrobials in pig	Creation of the focus group (20 experts)	2013
production	Develop and explore cost-effective integrated strategies to reduce the use of antibiotics	Publication final report in 2014 ⁹⁰
	Final report of the focus group.	

⁹⁰http://ec.europa.eu/eip/agriculture/en/content/animal-husbandry

G. Communication, education and training Action n° 12:		
Operational objectives	Concrete activities	Milestones / Deadline
Assess and improve the impact of the EU awareness and	European Antibiotic Awareness Day (EAAD) evaluation report	Publication of EAAD evaluation ⁹¹
communication initiatives on antimicrobial resistance	Annual EAAD stakeholder event and communication activities	EAAD marked annually by a stakeholder event and communication activities on and around 18 th November ⁹²
Monitor evolution of behaviour on antimicrobial resistance and prudent use in human medicine		Eurobarometer published and presented at the occasion of European Antibiotic Awareness Day 2013 ⁹³ Eurobarometer published and presented at Health Council June 2016 ⁹⁴ (Results in EU Member States) Eurobarometer published at the occasion of European Antibiotic Awareness Day 2016 ⁹⁵
Monitor evolution of behaviour on antimicrobial resistance and prudent use in veterinary medicine	In collaboration with relevant stakeholders identification of target groups and evaluation, (surveys, enquires, etc) on the impact and implementation of	On 11 September 2015 the European Commission published a Commission Notice on "Guidelines for the prudent use of antimicrobials in veterinary medicine" ⁹⁶
Conference Antimicrobial Resistance: Dissemination of information about EU approach on antimicrobial resistance	Mid-term review of the Commission's 5-year action plan against AMR with competent authorities of member states, international organizations and stakeholders representatives, focussing discussions on the challenges ahead, the drivers and possible limitations of the envisaged measures	Published December 2013 ⁹⁷
To inform about the progress made so far on the implementation of the Action Plan.	AMR Progress report	Published March 2015 ⁹⁸
To evaluate the impact and effectiveness of the measures taken and goals achieved by the implementation of the 5-year Action Plan	AMR evaluation report	Published October 2016 ⁹⁹

⁹¹http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20928
⁹²http://ecdc.europa.eu/on/EAAD/Pages/Home.aspx
⁹³http://ec.europa.eu/public_opinion/archives/ebs/ebs_407_en.pdf
⁹⁴http://ec.europa.eu/COMMFrontOffice/publicopinion/index.cfm/Survey/getSurveyDetail/instruments/SPECIAL/surveyKy/2107
⁹⁵Ongoing, link not available yet
⁹⁶http://ec.europa.eu/dgs/health_food-safety/amr/events/ev_20131211_en.htm
⁹⁸http://ec.europa.eu/health/antimicrobial_resistance/docs/2015_amr_progress_report_en.pdf
⁹⁹http://ec.europa.eu/dgs/health_food-safety/amr/action_eu/index_en.htm