



# 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 provisions of the Council Recommendation 2002/77/EC <sup>1</sup> in Member States, notably regarding: <ul style="list-style-type: none"> <li>• Prescription only requirements</li> <li>• Nursing homes and long term care facilities</li> <li>• Education and training programme</li> </ul>	Launch of the 2012-2014 preparatory action on Antimicrobial Resistance (grant from European Parliament) addressing <ul style="list-style-type: none"> <li>• Misuse of antimicrobial agents in human medicine</li> <li>• Awareness across the whole chain of stakeholders: prescribers, pharmacists and patients.</li> <li>• Sales of antimicrobial agents without a prescription</li> </ul>	2 <sup>nd</sup> quarter – 2014, start of the preparatory action on 'Antimicrobial Resistance and causes of non- prudent use of antibiotics in human medicine in the EU. (ARNA) 2 <sup>nd</sup> quarter – 2016, ARNA conference and completion of contract for preparatory action .
	Consultation with MS on the implementation of Council Recommendation 2002/77/EC.	Questionnaire sent out to Member States first half 2015  Preliminary results discussed with EU Health Security Committee November 2015. Report expected 1 <sup>st</sup> half 2016.
	Through the Antibiotic Prescribing and Resistance in European Children (ARPEC) <sup>2</sup> project 2010-2013 funded under Health Programme: development of web-based training providing educational modules on optimal antibiotic prescribing in children and antimicrobial resistance	Completed mid-2014.
Stimulate the appropriate use of antimicrobials in human medicines	Workshop “Best use of medicines legislation to bring new antibiotics to patients and combat the resistance problem”, organised by EMA (8 November 2013, London)  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	Workshop conclusions published (December 2013) <sup>3</sup>

<sup>1</sup> <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2002:034:0013:0016:EN:PDF>

<sup>2</sup> <http://www.arpecproject.eu/>

<sup>3</sup> [http://www.ema.europa.eu/ema/index.jsp?curl=pages/news\\_and\\_events/events/2013/09/event\\_detail\\_000781.jsp&mid=WC0b01ac058004d5c3](http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/events/2013/09/event_detail_000781.jsp&mid=WC0b01ac058004d5c3)

Research on improving the appropriate use of antimicrobials	The project " Genomics to combat Resistance against Antibiotics in Community acquired low respiratory tract infections in Europe" GRACE <sup>4</sup> project 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).	Publication in The Lancet Infectious Diseases <sup>5</sup>
	The EU Framework Programme for Research funded project "The appropriateness of prescribing antibiotics in primary health care in Europe with respect to antibiotics resistance" (APRES) <sup>6</sup> assesses the appropriateness of prescribing antibiotics in primary care in 9 European countries.	Project started in 2009 and final results were submitted in summer 2014 and a comprehensive related book "Antibiotic Treatment and Commensal Staphylococcus Aureus Resistance in Primary Care in Europe" was published <sup>7</sup>
<b>Action n° 2:</b>		
<b>Strengthen the regulatory framework on veterinary medicines and on medicated feed.</b>		
<b>Operational objectives</b>	<b>Concrete activities</b>	<b>Milestones / Deadline</b>
To address Antimicrobial Resistance related to the use of veterinary medicinal products	Revision of the Veterinary Medicines Legislation <sup>8</sup>	Veterinary Medicines legislation: Commission proposal adopted in 2014 and sent to the EP and the Council. Negotiations between the two institutions should take place at least until 2017.
To address Antimicrobial Resistance related to the use of medicated feed	Revision of the Medicated Feed Legislation <sup>9</sup> . Set harmonised limits for residues for veterinary medicines in non-target animal feed related to the production of medicated feed and possible other actions to address antimicrobial resistance related to the use of medicated feed.	Medicated Feed legislation: Commission proposal adopted in 2014 and sent to the EP and the Council.

<sup>4</sup> <http://www.grace-irti.org/portal/en-GB/homepage>

<sup>5</sup> Amoxicillin for acute lower-respiratory-tract infection in primary care when pneumonia is not suspected: a 12-country, randomised, placebo-controlled trial. Lancet Infect Dis. 2013 Feb;13(2):123-9

<sup>6</sup> [http://ec.europa.eu/research/health/public-health/clinical-outcome-into-practice/projects/apres\\_en.html](http://ec.europa.eu/research/health/public-health/clinical-outcome-into-practice/projects/apres_en.html)

<sup>7</sup> <https://www.nivel.nl/en/apres>

<sup>8</sup> [http://ec.europa.eu/health/veterinary-use/rev\\_frame\\_index\\_en.htm](http://ec.europa.eu/health/veterinary-use/rev_frame_index_en.htm)

<sup>9</sup> [http://ec.europa.eu/food/food/animalnutrition/labelling/medicated\\_feed\\_en.htm](http://ec.europa.eu/food/food/animalnutrition/labelling/medicated_feed_en.htm)

<p>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.</p>	<p>In relation to the distribution and use of antimicrobial veterinary medicinal products (including medicated premixes for animal feedingstuffs), the Food and Veterinary Office (FVO) shall send a questionnaire on this issue to all Member States in the second half of 2015 and, carry out a series of fact-finding missions in selected Member States in 2016. This FVO project will generate an overview report.</p>	<p>All Member States and stakeholders (Advisory Group on the Food Chain and Animal and Plant Health members and FVE member organizations) received the questionnaire in August 2015 with a response deadline of 16 November 2015. Nine fact finding missions in Member States to be completed during 2016; with a final overview report to be drafted by the first quarter of 2017.</p>
<p><b>Action n° 3:</b>  <b>Introduce recommendations for prudent use in veterinary medicine, including follow-up reports.</b></p>		
Operational objectives	Concrete activities	Milestones / Deadline
<p>Use existing legal tools to the utmost to ensure prudent use of antimicrobials in the veterinary</p>	<p>Commission decision on referral in relation to 3rd and 4th generation cephalosporins</p>	<p>Adopted on 13 January 2012, C(2012)182<sup>10</sup></p>
	<p>Scientific recommendations of the Committee for Medicinal Products for Veterinary Use (CVMP) on the need for further referrals of critically important antimicrobials<sup>11</sup></p>	<p>July 2013</p>
	<p>To initiate referrals on veterinary medicinal products taking into account the updated priority list for referrals as established by European Medicines Agency (EMA)</p>	<p>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 was converted into a Decision by the European Commission on 16 March 2015.</p> <p>In May 2015, referral was initiated on all veterinary medicinal products containing colistin in combination with other antimicrobial substances for oral administration</p>
<p>To have scientific recommendations on the use in the veterinary sector of last resort</p>	<p>Request for scientific advice (based on Article 57 of Regulation 726/2004) of Agency Committee for Medicinal Products for Veterinary Use (CVMP) and the Committee for Medicinal Products for Human Use (CHMP) on the</p>	<p>Published on 2014<sup>13</sup>          See also Action n° 7</p>

<sup>10</sup> [http://ec.europa.eu/health/documents/community-register/2012/20120113113370/dec\\_113370\\_en.pdf](http://ec.europa.eu/health/documents/community-register/2012/20120113113370/dec_113370_en.pdf)

<sup>11</sup> [http://www.ema.europa.eu/ema/index.jsp?curl=pages/news\\_and\\_events/news/2013/07/news\\_detail\\_001859.jsp&mid=WC0b01ac058004d5c1](http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2013/07/news_detail_001859.jsp&mid=WC0b01ac058004d5c1)

<sup>12</sup> [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/Scientific\\_guideline/2011/11/WC500118230.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2011/11/WC500118230.pdf)

<sup>13</sup> [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/Other/2013/04/WC500142070.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Other/2013/04/WC500142070.pdf)

antimicrobials for humans (e.g. tigecycline and colistin) sector	<p>use of last resort antimicrobials in the veterinary sector.</p> <p>Follow-up of the scientific recommendation published in 2014 prepared by the Antimicrobial Advice Ad Hoc Expert Group (AMEG)<sup>14</sup></p>	<p>A workshop is planned on 26.11.2015 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</p>
To reduce the overall use of antimicrobials in veterinary medicine (better targeted treatments, use according to best practices, etc)	<p>In addition to the legal provisions, development of a guidance document to provide overview of practical examples of prudent use principles to be considered implemented by Member States when developing national strategies on prudent use.</p> <p>Follow up reports of the implementation by Member States.</p>	<p>Guidance document on prudent use was published in March 2015.</p>
Guarantee responsible and efficient use of medicated feed	<p>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.</p>	<p>Current and follow-on to Action 2</p>
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.	<p>Questionnaire and fact-finding missions in selected Member States – see FVO project undertaken pursuant to Action No 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 FVO project referred to above.</p>	<p>All Member States and stakeholders (Advisory Group on the Food Chain and Animal and Plant Health members and FVE member organizations) received the questionnaire in August 2015 with a response deadline of 16 November 2015. Nine fact finding missions in Member States to be completed during 2016 with a final overview report to be drafted by the first quarter of 2017.</p>
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, third and fourth generation cephalosporins and macrolides).	<p>Evaluation of EU Member States' residue monitoring plans and supplementary assessment of Member States' screening methodology by the EU Reference Laboratory for antimicrobial residues</p>	<p>The evaluation of the 2013 residues monitoring plans was completed in November 2013 and the EURL assessment was provided in February 2014. An FVO discussion document has been finalised and published and presented to Member States and EU agencies at the AMR working group meeting of 1 July 2015.</p>

<sup>14</sup> [http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document\\_listing/document\\_listing\\_000385.jsp&mid=WC0b01ac058080a585](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000385.jsp&mid=WC0b01ac058080a585)

## B. Prevent microbial infections and their spread

### **Action n° 4:**

#### **Strengthen infection prevention and control in healthcare settings.**

Operational objectives	Concrete activities	Milestones / Deadline
Monitor and support the implementation of the Council Recommendation on patient safety incl. healthcare associated infections (HAI) with emphasis on: <ul style="list-style-type: none"> <li>• Development of guidance on infection prevention and control</li> <li>• Strengthened surveillance of HAI</li> <li>• Education and training of healthcare workers</li> <li>• Information to patients</li> </ul>	1st Report of the Commission on the implementation of the Council Recommendation on patient safety, including healthcare associated infections.	Adopted and published November 2012 <sup>15</sup>
	2nd Report of the Commission on the implementation of the Council Recommendation on patient safety, including healthcare associated infections.	Adopted and published 2014. <sup>16</sup>
	Support via the Health Programme projects/actions to follow up the priority areas on which future work should focus include, as identified in the Commission's implementation report	HAI prioritised in the Third Health Programme Project call issued in 2014
	Continue fostering with European Centre for Disease Prevention and Control (ECDC) the development of guidance on infection prevention and control, strengthening of Health Associated Infections (HAI) surveillance and the development of training curricula for healthcare workers.	Several guidance reports published <sup>17</sup>  Directory of existing guidance and other documents on the prevention and control of AMR and HAI online on ECDC website <sup>18</sup>

<sup>15</sup> [http://ec.europa.eu/health/patient\\_safety/docs/council\\_2009\\_report\\_en.pdf](http://ec.europa.eu/health/patient_safety/docs/council_2009_report_en.pdf)

<sup>16</sup> [http://ec.europa.eu/health/patient\\_safety/docs/ec\\_2ndreport\\_ps\\_implementation\\_en.pdf](http://ec.europa.eu/health/patient_safety/docs/ec_2ndreport_ps_implementation_en.pdf)

<sup>17</sup> <http://www.ecdc.europa.eu/en/Pages/home.aspx>

<sup>18</sup> [http://www.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](http://www.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)

<b>Action n° 5: Adoption of a proposal for an EU Animal Health Law.</b>		
<b>Operational objectives</b>	<b>Concrete activities</b>	<b>Milestones / Deadline</b>
<ul style="list-style-type: none"> <li>To create an animal health legal framework based on the principle "prevention is better than cure".</li> </ul>	<p>Animal Health Law proposal will foresee to:</p> <ul style="list-style-type: none"> <li>Increase responsibilities of operators to ensure the required level of animal health and biosecurity;</li> <li>clarify the responsibility of veterinary and aquatic animal health professionals to adopt effective measures to prevent the spread of pathogens and to raise awareness;</li> <li>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;</li> <li>provide for an assessment, prioritisation and categorisation of diseases or disease agents, including where appropriate, the ability to generate resistance to treatment as criterion to decide about appropriate measures;</li> <li>clarify obligations to ensure appropriate monitoring, surveillance and early detection of pathogens.</li> </ul>	<p>Final proposal was adopted by Commission on 6 May 2013<sup>19</sup>, it is in ordinary legislative procedure. The European Parliament and the Council reached political agreement on it on 1 June 2015<sup>20</sup> .. The text of the future Regulation is undergoing further procedural steps awaiting adoption by the co-legislators and subsequent publication in the Official Journal, likely to be around May 2016.</p> <p>Further details are foreseen in subsequent delegated and implementing acts as appropriate</p>

<sup>19</sup> COM(2013) 260 final, [http://ec.europa.eu/food/animal/animal-health-proposal-2013\\_en.htm](http://ec.europa.eu/food/animal/animal-health-proposal-2013_en.htm)

<sup>20</sup> [http://europa.eu/rapid/press-release STATEMENT-15-5091\\_en.htm](http://europa.eu/rapid/press-release_STATEMENT-15-5091_en.htm)

## 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 <sup>21</sup> projects are funded by the Commission, via Framework Programme 7 and Horizon 2020, and the European Federation of Pharmaceutical Industries and Associations ( <a href="http://www.imi.europa.eu">www.imi.europa.eu</a> )	in September 2015 IMI-2 launched its 6th Call
	To support the IMI project improving tests for appropriate use of antibiotics <sup>22</sup>	The project started in April 2011 for a duration of 60 months
	<p>The launch of a large IMI programme "new Drugs 4 Bad Bugs" that aims to bring new antibiotics to patients and currently covers:</p> <ol style="list-style-type: none"> <li>1) innovative trial design and clinical drug development</li> <li>2) learning from success and failure and getting drugs into bad bugs, and</li> <li>3) discovery and development of new drugs for combating Gram-negative infections</li> <li>4) Driving re-investment in R&amp;D and responsible use of antibiotics</li> <li>5) Clinical development of antibacterial agents for Gram-negative antibiotic resistant pathogens</li> <li>6) Systemic molecules against health care associated infections</li> <li>7) Inhaled anti-bacterials in bronchiectasis and cystic fibrosis</li> </ol> <p>This programme has a budget of more than €600 million</p>	<p>Two IMI Projects of the 6<sup>th</sup> call were launched in February 2013. COMBACTE pioneers new ways of designing and implementing efficient clinical trials for novel antibiotics<sup>23</sup> and TRANSLOCATION aims to increase the overall understanding of how to get antibiotics into multi-resistant Gram-negative bacteria<sup>24</sup> Project ENABLE<sup>25</sup> 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.</p> <p>ND4BB project DRIVE-AB<sup>26</sup> , 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.</p>

<sup>21</sup> <http://www.imi.europa.eu/>

<sup>22</sup> <http://www.imi.europa.eu/content/rapp-id>

<sup>23</sup> <http://www.imi.europa.eu/content/combacte>

<sup>24</sup> <http://www.imi.europa.eu/content/translocation>

<sup>25</sup> <http://www.imi.europa.eu/content/enable>

<sup>26</sup> <http://drive-ab.eu/>

		<p>In February 2015, COMBACTE-MAGNET 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<sup>27</sup>.</p> <p>The latest project, jABC, started in August 2015 and will develop two inhaled antibiotics to help cystic fibrosis and bronchiectasis patients.</p> <p>Proposal evaluation/ contract negotiations of additional projects going on in 2015.</p>
<p>To assess the possibilities for increasing the efficiency of the market authorisation process in relation to new antibiotics</p>	<p>To launch a dialogue with the health authorities of the Member States and other relevant stakeholders in view of a co-ordinated approach to introduce incentives for the development and marketing of new antibiotics</p>	<p>Event on the best use of medicines legislation to bring new antibiotics to patients and combat the resistance problem (8 November 2013)</p> <p>EMA workshop on the use of pharmacokinetics and pharmacodynamics in the development of antibacterial medicinal products (12-13 November 2015)</p> <p>Ongoing discussions with EMA &amp; STAMP for optimisation of existing regulatory tools for all medicines, including antibiotics.</p>
	<p>To complete an assessment of relevant non-legislative market authorisation process aspects in view of streamlining and accelerating the introduction of new antibiotics.</p> <p>New EMA Guidance on the use of pharmacokinetics and pharmacodynamics analyses in the development of antibiotics in public consultation til 31 March 2016.</p>	
	<p>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</p>	
<p><b>Action n° 7:</b>  <b>Promote efforts to analyse the need for new antibiotics into veterinary medicine.</b></p>		
<p><b>Operational objectives</b></p>	<p><b>Concrete activities</b></p>	<p><b>Milestones / Deadline</b></p>

<sup>27</sup> <http://www.combacte.com/News/News-Publications/ID/26/Launch-COMBACTE-MAGNET>

To analyse the need for new antibiotics into veterinary medicine	To have scientific advice of European Medicines Agency (Committee for Medicinal Products for Veterinary Use (CVMP) and the Committee for Medicinal Products for Human Use (CHMP)) whether new classes of veterinary antimicrobials contribute to having a better management of the development of AMR and these new classes could be used in the veterinary sector or should be set aside for human use	Report published 2014 <sup>28</sup> See also Action 3
	Follow-up of the scientific recommendation published in 2014 prepared by the Antimicrobial Advice Ad Hoc Expert Group (AMEG)	A workshop is planned on 26.11.2015 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
To facilitate the use of alternatives that may reduce the need for treatment with antimicrobials	Reducing the need for antimicrobials by using specific feed materials and authorised feed additives e.g. with possible effects on the gut flora	Authorisation of additives is dependent on applications received

<sup>28</sup> [http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document\\_listing/document\\_listing\\_000385.jsp&mid=WC0b01ac058080a585](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000385.jsp&mid=WC0b01ac058080a585)

## 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 AMR.	Implementation of the 17 Transatlantic Taskforce Antimicrobial Resistance (TATFAR) Recommendations <sup>29</sup>	TATFAR progress report published May 2014 <sup>30</sup>
	Bi-annual TATFAR audio-conference meetings and organisation of a face-to-face meeting with part of the group to review progress and discuss follow-up (depending on available funding)	Face-to-face meeting during of TATFAR group took place on 22-23/10/2015 in associated event of the Luxembourgish Presidency.
	End of 2013, TATFAR was prolonged until the end of 2015, 15 of the recommendations will continue, one new recommendation has been added.	TATFAR Work plan for 2016-2020 expected adoption 1 <sup>st</sup> quarter 2016.
Discussion with international partners identifying areas of cooperation	Cooperation and joint actions in the fields of surveillance, promotion of prudent use of antimicrobials, awareness/communication and healthcare-related infection prevention and control.	
	Bilateral cooperation China-EU	1st Seminar China-EU (Beijing) March 2013 2nd Seminar China-EU (first half 2015) Comparative studies on policies (ongoing)
	Bilateral cooperation Russian Federation-EU	AMR as standing item of meetings of the Russian Federation Sub-group on Communicable Diseases (on hold)

<sup>29</sup> <http://www.ecdc.europa.eu/en/activities/diseaseprogrammes/tatfar/Pages/index.aspx?MasterPage=1>

<sup>30</sup> <http://www.cdc.gov/drugresistance/tatfar/index.html>

World Health Organisation (WHO)	Cooperation with WHO to support development of WHO Global Action Plan	Participation to WHO meetings related to the development of the WHO Global Action Plan Provide input to WHO consultation on global action plan
Implementation of the World Health Organisation (WHO/EURO)-DG Health and Food Safety “Health Security Roadmap” identifying Antimicrobial Resistance as an area for cooperation”	Annual WHO-EURO / EC Senior officials meetings reviewing WHO/EURO-DG Health and Food Safety “Health Security Roadmap”	WHO-EC meeting May 2013 WHO-EC meeting June 2014 WHO-EC meeting February 2015
	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 Organization for Animal Health (OIE)	Support to the Conference on Antimicrobial Resistance organized by the World Organization 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 OECD conference on AMR	2015-2016 grant (Third Health Programme) The meeting took place on 12/10/2015
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 2016-2017
Rationale use of medicines through the Renewed Partnership EU-WHO in 15 countries <sup>31</sup>	1) Provide technical assistance to countries to update their list of essential medicines, their Standard Treatment Guidelines and their National Formulary  2) Provide technical assistance to countries to survey prescribing,	Depends on the countries (x15)- below some examples:  a)Burundi: Training of trainers on the use of guidelines for medicinal products in health centers

<sup>31</sup> Burundi ; Cameroon ; Congo ; DRC ; Ethiopia ; Ghana ; Guinea-Conakry ; Kenya ; Mali ; Mozambique ; Senegal ; Tanzania ; Togo ; Zambia ; Zimbabwe.

	<p>dispensing and use of medicines using WHO methodology- Done in Ghana</p> <p>3) 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 use</p>	<p>b) DRC: Perform a survey of prescribing practices, dispensing and use of antibiotics in the Eastern Region.</p> <p>c) Ghana: Develop surveillance system for antibiotic use in three in hospitals. Train staff to use the system to collect data on antibiotic use.</p>
<p>Local capacity building and awareness campaigns through a comprehensive support to national policy and Plans</p>	<p>Health is a sector of concentration in 17 countries<sup>32</sup>. The DEVCO 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.</p>	<p>On-going with the development of the activities under the 11<sup>th</sup> European Development Fund (EFD)</p>

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<sup>32</sup> Burkina 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 through:	Ensuring the sustainability of the European Surveillance system of Antimicrobial Consumption (ESAC). Transfer of European Surveillance system of Antimicrobial Consumption to European Centre for Disease Prevention and Control	Completed December 2012
	Publication of ESAC reports Publication of EARS-net reports Publication of point prevalence surveys	Several ESAC reports published EARS-net reports published November each year
	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). <sup>33</sup>	Decision adopted 2012.  Monitor of the implementation: by December 2015
	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 <sup>34</sup>	Completed 2014.

### **Action n° 10:**

**Strengthen surveillance systems on AMR and antimicrobial consumption in animal medicine.**

Operational objectives	Concrete activities	Milestones / Deadline
Harmonized surveillance systems and monitoring on the occurrence of antimicrobial resistance and consumption of antimicrobials will	European. Surveillance of Veterinary Antimicrobial Consumption (ESVAC) <sup>35</sup> project coordinated by the European Medicines Agency on collection data on the consumption of antimicrobials on a multiphase approach:	

<sup>33</sup> <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2012:262:0001:0057:EN:PDF>

<sup>34</sup> <http://www.arpecproject.eu/>

<sup>35</sup> [http://www.emea.europa.eu/ema/index.jsp?curl=pages/regulation/document\\_listing/document\\_listing\\_000302.jsp&mid=WC0b01ac0580153a00](http://www.emea.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000302.jsp&mid=WC0b01ac0580153a00)

<p>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.</p>	<ul style="list-style-type: none"> <li>• Pilot project collecting standardized overall sales data</li> <li>• Collecting and report overall national sales data from all Member States</li> </ul> <p>Reinforce legal base for collection of antimicrobials in regulatory framework for veterinary medicines</p>	<ul style="list-style-type: none"> <li>• 5<sup>th</sup> ESVAC report was published in October 2015 – on sales in 2013 (24 Member States and 2 EEA countries provided data: 2 more Member States recently joined the project and provided data for 2014.</li> <li>• 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.</li> </ul> <p>Legal proposal for review of veterinary medicines 2014 (see Action 2)</p>
<p>Harmonized surveillance systems 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.</p>	<p>Harmonization of surveillance and monitoring of antimicrobial resistance in the food chain:</p> <ul style="list-style-type: none"> <li>• Request of scientific and technical assistance to the European Food Safety Authority (EFSA) on harmonizing monitoring in bacteria transmitted through food.</li> <li>• New legal framework for harmonised monitoring of antimicrobial resistance in zoonotic and commensal bacteria in the food chain.</li> <li>• Financial contribution from the Union to the harmonized monitoring of AMR carried out by the Member States.</li> <li>• Request of scientific and technical assistance to the European Food Safety Authority (EFSA) on randomisation of sampling for the purpose of AMR monitoring</li> </ul>	<p>EFSA opinion on harmonization monitoring AMR published in 2012<sup>36</sup></p> <p>Decision 2013/652/EU<sup>37</sup> on harmonised monitoring and reporting of antimicrobial resistance in the food chain in the EU.</p> <p>Decision 2013/653/EU<sup>38</sup> 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.</p> <p>EFSA opinion on randomisation of sampling for monitoring AMR published in May 2014<sup>39</sup></p>

<sup>36</sup> <http://www.efsa.europa.eu/en/efsajournal/pub/2742.htm> and <http://www.efsa.europa.eu/en/efsajournal/pub/2897.htm>

<sup>37</sup> <http://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1403594558125&uri=CELEX:32013D0652>

<sup>38</sup> <http://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1403594663786&uri=CELEX:32013D0653>

<sup>39</sup> <http://www.efsa.europa.eu/de/efsajournal/pub/3686.htm>

<p>Surveillance and monitoring of the occurrence of pathogens in the framework of Animal Health Law          No treatment of animals without proper diagnosis; in particular treatment should not jeopardize detection of certain major pathogens.</p>	<p>Animal Health Law proposal</p>	<p>The same as for Action nr 5</p>
<p>To verify on-the spot that Member States comply with the legislation on monitoring of AMR. Identify good practices. Gather information on voluntary monitoring systems.</p>	<p>Two pilot audits (to develop approach in this area).           A series of targeted audits in 6 representative Member States (issuing of individual reports after each audit with recommendations).           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).</p>	<p>Two pilot audits in the autumn 2015:          -Denmark from 15 to 22 September          -Germany from 10 to 20 November          Six audits in Member States to be completed by the end of 2016.           Overview report by the end of first quarter 2017</p>
<p>The information on antimicrobial resistance and antimicrobial consumption collected by the three agencies EFSA, EMA and ECDC needs to be combined and analysed in order to allow a clear identification and quantification of the risk of developing and spreading antibiotic resistance in the food chain.</p>	<p>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 Resistance Analysis Report (JIACRA).</p>	<p>First JIACRA report published January 2015<sup>40</sup>           The second JIACRA report has been provisionally foreseen at the end of 2017, with a possibility of issuing interim reports in between..</p>

<sup>40</sup> [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/Report/2009/10/WC500004306.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Report/2009/10/WC500004306.pdf)  
<http://www.efsa.europa.eu/en/efsajournal/pub/4006.htm>  
<http://www.ecdc.europa.eu/en/publications/Publications/antimicrobial-resistance-JIACRA-report.pdf>

## F. Additional Research and Innovation

### **Action n° 11:**

**Reinforce and co-ordinate research efforts. Innovation.**

Operational objectives	Concrete activities	Milestones / Deadline
Reinforce antimicrobial resistance research in a coordinated fashion in three different thematic areas within the last calls of the seventh Framework Programme for Research:	<p>An overview of research projects related to drug resistance can be found: <a href="http://ec.europa.eu/research/health/infectious-diseases/antimicrobial-drug-resistance/index_en.html">http://ec.europa.eu/research/health/infectious-diseases/antimicrobial-drug-resistance/index_en.html</a></p> <p>Under the 7th Framework Programme the European Commission has published Research Work Programmes in which call topics on AMR were published in a coordinated manner:</p> <ul style="list-style-type: none"> <li>• HEALTH Work Programme (WP) (<a href="ftp://ftp.cordis.europa.eu/pub/fp7/health/docs/fp7-health-wp-2013_en.pdf">ftp://ftp.cordis.europa.eu/pub/fp7/health/docs/fp7-health-wp-2013_en.pdf</a>),</li> <li>• KBBE Work Programme (<a href="ftp://ftp.cordis.europa.eu/pub/fp7/docs/wp/cooperation/kbbe/b-wp-201301_en.pdf">ftp://ftp.cordis.europa.eu/pub/fp7/docs/wp/cooperation/kbbe/b-wp-201301_en.pdf</a>) and the</li> <li>• NMP Work programme (<a href="ftp://ftp.cordis.europa.eu/pub/fp7/docs/wp/cooperation/nmp/d-wp-201101_en.pdf">ftp://ftp.cordis.europa.eu/pub/fp7/docs/wp/cooperation/nmp/d-wp-201101_en.pdf</a>)</li> </ul>	2007 -2013
	The codes below refer to the call topics in the Work Programmes:	
Antimicrobial transfer throughout the food chain	<ul style="list-style-type: none"> <li>• WP2013, call7, topic KBBE.2013.1.3-05 for €9Mio EU contribution</li> </ul>	Project EFFORT, which studies the ecology and transmission of AMR from farm to fork, started Dec 2013
Antimicrobial resistance in farming and animal production	<ul style="list-style-type: none"> <li>• WP2012, call6, topics KBBE.2012.1.2-10 &amp; KBBE.2012.1.4-04;</li> </ul>	Projects on Impact matrix analysis and cost-benefit calculations to improve management practices regarding health status in organic dairy farming ("IMPRO" <sup>41</sup> ) and on Targeted disease prophylaxis in European fish farming ("TARGETFISH" <sup>42</sup> ;) projects started 4th quarter 2012.

<sup>41</sup> <http://www.dev.impro-dairy.eu/index.php/fr/>

<sup>42</sup> <http://www.wageningenur.nl/en/show/TARGETFISH.htm>

<p>Development of diagnostic tools for infectious diseases</p>	<ul style="list-style-type: none"> <li>• WP2013, call7, KBBE topics KBBE.2013.1.1-01, KBBE.2013.1.3-03, KBBE.2013.3.5-01 for a total of €21Mio EU contribution</li> </ul>	<p>Projects related to " Routine diagnostic tool for urinary tract infections caused by extended spectrum beta lactamase and carbapenamase producing bacteria" (ROUTINE) and to "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) are in particular related to drug resistance and started in 2012.</p>
	<ul style="list-style-type: none"> <li>• HEALTH.2012.2.3.0-1</li> </ul>	
	<ul style="list-style-type: none"> <li>• PHC-12-2015 (SME Instrument)</li> </ul>	<p>2 Projects will be 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.</p>

	<ul style="list-style-type: none"> <li>HOA 8 – 2015: Inducement Prize</li> </ul>	<p>The EC will launch 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<sup>43</sup>. Award decision: 2016.</p>
Mobilise Small and medium enterprise (SME) to develop new antimicrobials and vaccines;	<ul style="list-style-type: none"> <li>HEALTH.2013.2.3.1-1</li> </ul>	<p>7 Projects to support research and development of drugs, vaccines or alternative treatments for bacterial infections have been funded<sup>44</sup> The work of 44 innovative SMEs will be directly supported</p>
Research to the use of antimicrobials via personalised approaches	<ul style="list-style-type: none"> <li>HEALTH.2013.2.3.1-2</li> </ul>	<p>4 other funded projects seek to identify better methods to use currently available antibiotics.</p>
Developing novel nanotechnology enabled therapies for bacterial infectious diseases	<ul style="list-style-type: none"> <li>NMP.2013.1.2-2</li> <li>HEALTH. 2012.2.3.1-1</li> </ul>	<p>Another 4 projects study the usage of novel nano technology for drug delivery.</p>
Support the Joint Programming Initiative (JPI) on Antimicrobial Resistance (AMR)		<p>Participation in the Management Board of the JPI AMR as a non-voting member and funding for the implementation of this JPI via a coordination and support action (since end 2012), first call launched Jan 2014 JPIAMR Strategic Research Agenda launched 3 April 2014</p>
	<ul style="list-style-type: none"> <li>HCO 12 – 2015: ERA-NET</li> </ul>	<p>First H2020 WP published at the end of 2013 EC support of transnational research calls of JPIAMR via ERA-NET Co-fund scheme. The 2<sup>nd</sup> transnational call is closed since May 16.</p>
	<ul style="list-style-type: none"> <li>1st transnational call: InnovaResistance <a href="http://www.jpjamr.eu/activities/open-call/">http://www.jpjamr.eu/activities/open-call/</a></li> <li>2<sup>nd</sup> 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".</li> </ul>	<p>Proposals were submitted. Evaluation is underway. Then next call will be launched in January 2016.</p>

<sup>43</sup> [www.ec.europa.eu/horizonprize/antibiotics](http://www.ec.europa.eu/horizonprize/antibiotics)

<sup>44</sup> [http://europa.eu/rapid/press-release MEMO-13-996\\_en.htm?locale=en](http://europa.eu/rapid/press-release_MEMO-13-996_en.htm?locale=en)

Contribute to a global mapping of drug resistance	<ul style="list-style-type: none"> <li>• H2020 WP 2014-15</li> </ul>	Meeting between the World Health Organisation (WHO) and the European Commission ( EC) in January 2012, participation in WHO Advisory Group 2013
	<ul style="list-style-type: none"> <li>• Cooperation and joint actions in the field of global mapping</li> </ul>	
Foster Innovation-Focus group on reduction of antimicrobials in pig production	Creation of the focus group (20 experts).	2013
	Develop and explore cost-effective integrated strategies to reduce the use of antibiotics. Final report of the focus group.	Publication final report in 2014 <sup>45</sup>

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<sup>45</sup> <http://ec.europa.eu/eip/agriculture/en/content/animal-husbandry>

## G. Communication, education and training

### Action n° 12:

#### Communication, education and training: Survey and comparative effectiveness research.

Operational objectives	Concrete activities	Milestones / Deadline
Assess and improve the impact of the EU awareness and communication initiatives on antimicrobial resistance	European Antibiotic Awareness Day (EAAD) evaluation report	Publication of EAAD evaluation report <sup>46</sup>
	Annual EAAD stakeholder event and communication activities	EAAD marked annually around 18 <sup>th</sup> November <sup>47</sup>
Monitor evolution of behaviour on antimicrobial resistance and prudent use in human medicine	3 <sup>rd</sup> Eurobarometer Survey on antimicrobial resistance	Eurobarometer published and presented at the occasion of European Antibiotic Awareness Day 2013 <sup>48</sup>
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 campaigns on prudent use antimicrobials, awareness, etc.	On 11.9.2015 the European Commission published a Commission Notice on "Guidelines for the prudent use of antimicrobials in veterinary medicine" <sup>49</sup>
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.	11 December 2013 <sup>50</sup>
To inform about the progress made so far on the implementation of the Action Plan.	AMR Progress report	Published March 2015 <sup>51</sup>

<sup>46</sup> <http://ecdc.europa.eu/en/eaad/Pages/Home.aspx>

<sup>47</sup> <http://ecdc.europa.eu/en/EAAD/Pages/Home.aspx>

<sup>48</sup> [http://ec.europa.eu/public\\_opinion/archives/ebs/ebs\\_407\\_en.pdf](http://ec.europa.eu/public_opinion/archives/ebs/ebs_407_en.pdf)

<sup>49</sup> [http://ec.europa.eu/health/antimicrobial\\_resistance/docs/2015\\_prudent\\_use\\_guidelines\\_en.pdf](http://ec.europa.eu/health/antimicrobial_resistance/docs/2015_prudent_use_guidelines_en.pdf)

<sup>50</sup> [http://ec.europa.eu/health/antimicrobial\\_resistance/events/ev\\_11122013\\_en.htm](http://ec.europa.eu/health/antimicrobial_resistance/events/ev_11122013_en.htm)

<sup>51</sup> [http://ec.europa.eu/health/antimicrobial\\_resistance/docs/2015\\_amr\\_progress\\_report\\_en.pdf](http://ec.europa.eu/health/antimicrobial_resistance/docs/2015_amr_progress_report_en.pdf)

To evaluate the impact and effectiveness of the measures taken and goals achieved by the implementation of the 5-year Action Plan

Ex-post evaluation

By mid 2016