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Act now – Antibiotics and Antibiotic resistance in the environment

Workshop Report of a workshop held in Brussels on November 7, 2018

by

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List of Abbreviations

AMR	Antimicrobial Resistance
COM	EU Commission
DG Environment	Directorate-General for the Environment
DG Santé	Directorate-General for Health and Food Safety
ECDC	European Centre for Disease Prevention and Control
EEA	European Economic Area
EFSA	European Food Safety Authority
EMA	European Medicines Agency
EQS	Environmental quality standard
ESBL	Extended-spectrum beta-lactamase
FAO	Food and Agriculture Organisation of the United Nations
GMP	Good Manufacturing Practice (for pharmaceuticals)
MEP	Member of the European Parliament
MSs	Member States (of the EU)
N	Nitrogen
OHAP	EU One Health Action Plan (against antimicrobial resistance)
P	Phosphorus
PE	Population Equivalent
REACH	Regulation concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals
UBA	Umweltbundesamt - German Environment Agency
UWWTD	Urban Waste Water Treatment Directive
WFD	Water Framework Directive
WHO	World Health Organisation
WWTPs	Waste water treatment plants

1 Background

In June 2017, the EU Commission adopted the new EU One Health Action Plan to combat antimicrobial resistance (AMR). The "One Health" approach which lies at the basis of the Action Plan is centred on an integrative management of health risks; it leaves aside a purely human or veterinary approach in favour of a more holistic one which includes the environment.

In this context, the German Environment Agency prepared a background paper which presents 28 options for action in seven areas: prevention, communication, authorisation, wastewater treatment plants, environmental waters, agriculture and soil. The aim is to support the overarching objective of the EU One Health Action Plan: against the background of growing problems with antibiotic resistance, the aim is to maintain the possibility of effective infection treatment in humans and animals.

On November 7, 2018, an international workshop titled "Act Now - Antibiotics and Antibiotic Resistance in the Environment" was held in Brussels, Belgium. The over 50 participants included representatives from the EU Parliament, national regulatory agencies, the pharmaceutical industry, the water industry, and NGOs, amongst others.

The workshop had two main aims: disseminating amongst relevant parties the latest scientific knowledge on antimicrobial resistance and its transmission in the environment, and fostering exchanges between actors on the conditions and possibilities for incorporating the options for action identified by the German Environment Agency into different actions and strategies, for instance at the EU level. The workshop was divided into four parts:

1. Plenary presentations presenting the state-of-knowledge on the topic, the identified options for action, and the status of current legislative initiatives.
2. A plenary discussion between presenters and participants.
3. A World Café section, identifying the aforementioned conditions and possibilities for take-up of options.
4. A final summary of the World Café results in the plenary.

This report presents key points of the plenary presentations, summarises the main points of the first podium discussion, and provides an overview of the discussions in the three World Café tables. The workshop agenda is included in Annex I, and the list of participants in Annex II.

2 Plenary session

Ms Jutta Klasen, of the **German Environment Agency,** and **Mr Viktor Szontagh** of the **Permanent Representation of Austria in the EU,** welcomed the workshop participants.

2.1 *"Multi-drug resistance as a growing global problem and its impacts in Germany"*

Prof. Christoph Lübbert, Department of Infectious Diseases and Tropical Medicine, University Hospital Leipzig

The processes conducing to antibiotic resistance have always existed, as analysis of genetic material in quaternary deposits ca. 30,000 years old has shown. These same processes are at work in the present day and era. After the identification of the first antibiotics in the 1930s and 1940s, it was only a few years before the first cases of resistance were documented (e.g. first sulphonamides discovered in the mid-1930s, first report of sulphonamide resistance in 1942; penicillin discovered in 1928 and approved in 1941, first identification of penicillin-resistant Staphylococcus aureus in 1949). The qualitative and quantitative use of antibiotics is equivalent to the development of resistance. Professor Lübbert highlighted that this is a natural law!

There is also a link between the proliferation of antibiotic resistance and a country's health system and overall governance. Studies have shown that there is a correlation between countries with worse governance (measured in terms of control of corruption) and average antibiotic resistance. Within Europe there are enormous differences, with one study quantifying the yearly deaths due to infections with antibiotic resistant bacteria at 10,700 for Italy to around 200 in the Netherlands, and only 15 in Estonia. For the EU/EEA, this same study lists a total of ca. 33,100 yearly deaths. The worldwide estimate of deaths due to AMR in the present day is of 700,000; an overrated forecast for the year 2050 by O'Neill (from the UK) is 10 million extra deaths per year, more than those due to cancer today (8.2 million)!! The two main causes of AMR are human and animal antimicrobial misuse or overuse.

Studies have shown that there is a link between the spread of resistance genes and travel. Research on extended-spectrum beta-lactamase (ESBL) producing bacteria (beta-lactamase has the ability to break down common antibiotics such as penicillins and cephalosporins) have shown that the acquisition and spread of these bacteria as a result of international travel is substantial and worrisome. A significant percentage of travellers acquire these bacteria while travelling through a region; the highest rate was measured for India, with 89% of travellers acquiring ESBL producing bacteria. What is particularly worrisome is the import of multi-drug resistant bacteria through patients hospitalised abroad. In the University Hospital Leipzig, where Professor Lübbert leads the Department of Infectious Diseases and Tropical Medicine, 105 patients were infected in 2010 to 2012 with a strain of multi-drug resistant bacteria imported by a patient who had been hospitalised in Rhodes, Greece. Of these 105 patients, 44 died.

Professor Lübbert then talked about the field research he conducted in India, in which amongst other things water samples were taken in rivers to which pharmaceutical industries discharge their production waters. India is one of the largest producer of medicines, with over 60% of the global vaccine production and over 60% of the world's antiretroviral drugs. Different UN organisations source their medicines to an enormous degree in the country. However, the side effect of this production is for instance high levels of fluoroquinolones in the aquatic environment, due to effluent discharges from bulk drug manufacturers, leading to the spread of resistances in the environment. A further consequence is that fish from around Hyderabad is not suitable to be used for human consumption. Mass fish deaths have also been associated with the discharges of the pharmaceutical industry.

Professor Lübbert's personal conclusion is that it is not fair that Europe is outsourcing dirty antibiotic manufacturing processes to emerging countries that already have the biggest antibiotic resistance problems worldwide. He appeals to the European Commission for its commitment to ensure that the pharmaceutical industry transparently discloses its supply chains and to strictly prevent the release of antibiotics into the environment. In his opinion, this can only be achieved through a redefinition of the Good Manufacturing Practice (GMP) criteria under the auspices of the WHO, with the addition of globally harmonized environmental standards as part of the regulatory controls for pharmaceutical products, in particular antibiotics and chemotherapeutics.

2.2 *"The EU Commission's Strategic Approach to Pharmaceuticals in the Environment"*

Helen Clayton, Policy Officer DG Environment, Unit C.1 "Clean Water", European Commission

Ms Clayton began by explaining how the requirement for the European Commission to develop a Strategic Approach to Pharmaceuticals in the Environment had arisen. She noted that the Commission's original proposal from 2011 to list three pharmaceuticals as priority substances had not been supported by the Council, and that the Parliament had proposed a compromise to address the risk from pharmaceuticals more generally. A study already commissioned by DG Santé had led to the publication of a report in 2014 on pharmaceuticals in the environment, and this was being complemented by a second study to inform the Strategic Approach. The roadmap for the initiative had been subject to public consultation in 2017, and additional public and targeted stakeholder consultations had been launched in late 2017 to gather views and information on a range of policy options for possible inclusion in the Strategic Approach. The report of the study, including the results of the consultations, would soon be published.

Ms Clayton noted that the results of the public consultation showed most respondents considered there to be a link between the presence of pharmaceuticals in the environment and antimicrobial resistance. She stressed the relevance of the Strategic Approach to achieving some of the objectives of the updated EU Action Plan on Antimicrobial Resistance. She noted that although there is a need to obtain more information on the role of the environment in antimicrobial resistance, it is also appropriate to already identify actions to reduce the emissions of antimicrobials.

Finally, she referred to a recent action to add two more antibiotics (on top of the three already included) to the surface water Watch List under the Water Framework Directive, and mentioned that some monitoring of antibiotics in soil is also planned as part of another initiative.

2.3 *"The European One Health Action Plan against Antimicrobial Resistance"*

Aurélien Perez, Policy Officer DG Santé, European Commission

Antimicrobial resistance (AMR) is the ability of microorganisms to resist antimicrobial treatments, especially antibiotics. AMR has a direct impact on human and animal health and carries a heavy economic burden due to higher costs of treatments and reduced productivity caused by sickness. A recent study estimates that about 33,000 people die each year in the EU/EEA as a direct consequence of an infection due to bacteria resistant to antibiotics.

Over the last 15 years, the EU has deployed a lot of efforts in tackling antimicrobial resistance, as the 2001 Community Strategy against Antimicrobial Resistance shows. This policy was reinforced with the 2011 Commission Action Plan.

In June 2017, the Commission adopted the EU One Health Action Plan against AMR, as requested by the Member States in the Council Conclusions of 17 June 2016. It builds on the 2011 Action Plan, its evaluation, the feedback received on a European Commission Roadmap on AMR and an open public consultation.

The key objectives of the 2017 action plan are built on three main pillars:

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

The Commission has started delivering on the actions contained in the 2017 Action Plan (e.g. EU guidelines on prudent use of antimicrobials in human health published in July 2017, joint action on AMR and healthcare-associated infections started in September 2017, 2nd Joint Inter-agency (EMA / EFSA / ECDC) report on Antimicrobial Consumption and Resistance Analysis published in July 2017, one-health AMR visits in Member States started in June 2017, AMR training for Competent Authorities started in November 2017, AMR training in third countries launched in September 2018, EU Joint Action on vaccination which came into force in August 2018, audits of EU legislation on AMR monitoring in food/animals, fact-finding missions in Member States on prudent use of antimicrobials in animals).

Two progress reports were already published, on February 21 and September 26, 2018 respectively, and will be regularly updated.

The state of play of implementation of the 2017 Action Plan is regularly presented to the AMR One Health Network.

2.4 *"Environment in the One Health Action Plan of the European Parliament"* Karin Kadenbach, MEP, Rapporteur in the European Parliament on the EU's One Health Action Plan against Antimicrobial Resistance

Why is this fight against antimicrobial resistance so important? Because nearly 500 people in the European Union die every week from infections caused by multidrug-resistant bacteria. Ms Kadenbach asked participants to imagine if this number of people would be dying regularly in plane crashes: if a plane were to be coming down every two or three days with no survivors, the outcry would be considerably louder.

Ms Kadenbach pointed out the paragraphs in which the Parliament report **"European One Health Action Plan against Antimicrobial Resistance (AMR)"** speaks in particular about the environment and water. A selection:

The report states for instance in the first paragraph that the "**One Health Principle"** must play a central role in tackling AMR. The health of people and animals and the environment are interconnected and diseases are transmitted from people to animals and vice versa.

The report also asks that an EU strategy **for tackling drug residues** in water and the environment must be drawn up immediately. The Commission has not yet proposed a strategic approach on pharmaceuticals polluting water, as required by the Water Framework Directive. Furthermore, the importance and usefulness of an integrated chain approach to drug residues and AMR in the environment is stated.

It is also highlighted in the report that the pollution of the environment by human and animal **antibiotic residues**, particularly by livestock farming, hospitals and households, is an emerging problem that requires coherent policy measures to prevent the spread of AMR among ecosystems, animals and

people. It is therefore necessary to encourage further research into transmission dynamics and the relative impact of this pollution on AMR. For such research it is important to develop and use the synergies between the One Health approach and the existing environment monitoring data.

The report also asks that the Commission should take appropriate steps to address the **release of pharmaceuticals**, including antimicrobials, **into the environment** through both wastewater and wastewater treatment plants, as a major factor in the emergence of AMR.

The European Parliament is calling on the Commission and the member states to encourage the development of **sustainable medicinal products** with a low impact on the environment and water supplies, and to encourage further innovation in the pharmaceutical industry in this area.

The Commission and Member States are called to set **quality standards** (threshold values) or risk assessment requirements to ensure that manure, sewage sludge and irrigation water contain safe concentrations of relevant antibiotics and AMR microorganisms before they can be used on agricultural fields.

2.5 *"Options to minimise antibiotics and antibiotic resistance in the environment"* Jutta Klasen, Head of Chemical Safety Division, German Environment Agency (UBA)

The EU "One Health Action Plan on antimicrobial resistance (AMR)" contains measures to combat AMR mainly in the areas of human and veterinary health. Although the role of AMR in the environment was recognized, only limited measures were considered in this respect in the plan.

To fill this gap, the German Environment Agency prepared a background paper on antibiotics and AMR in the environment, which summarises the scientific knowledge and proposes seven areas of activities with a set of specific measures.[1]

Large amounts of antibiotics used in human and veterinary medicine enter the environment through waste water and organic fertilisers. Environmental entry paths are identical for antibiotics and AMR. Indeed, antibiotics and antimicrobial resistance have been reported in all environmental compartments, thus building a reservoir of AMR. Even low concentrations of antibiotics increase the selective pressure and thereby promote AMR development. Besides, antibiotics can harm aquatic and soil organisms and thus entire ecosystems.

In view of this, the background paper proposes concrete measures – including the technical upgrade of wastewater treatment plants, linking the quantities of antibiotics used in livestock production with the documentation of manure parameters, the transfer of this information from manure production via fermentation to application on soils, as well as a systematic monitoring of antibiotics and AMR in the environment.

Due to the relevance and urgency of this global problem, as many concrete measures from this compilation as possible should be implemented as soon as possible, in order to reduce antibiotics and AMR in the environment.

[1] Umweltbundesamt (2018). Antibiotics and Antibiotic Resistances in the Environment - Background, Challenges and Options for Action. https://www.umweltbundesamt.de/publikationen/antibiotics-antibiotic-resistances-in-the

3 Plenary discussion

- The plenary discussion focused on the **"Potential of and synergies between the EU initiatives from the perspective of antibiotics and antimicrobial resistance".** The five presenters (Prof. Lübbert, Helen Clayton, Aurélien Perez, Karin Kadenbach, Jutta Klasen) were part of the podium, taking questions from the plenary.
- The discussions started on the role of upcoming documents and reviews on the EU level. The question was raised by a regulator on how the EU Commission (COM) will act in regard of the Water Framework Directive, the EU's Strategic Approach to Pharmaceuticals in the Environment and the results of the One Health Action Plan. The regulator also asked if AMR in soil is an issue. Helen Clayton from DG Environment highlighted that antimicrobial resistance is not mentioned in the Water Framework Directive, which is substance related. Therefore, only antibiotics (as compounds) can be discussed under the WFD. According to Ms Clayton, antibiotics in soil are not an issue so far; the question of if antibiotics can be found in soil still needs to be answered. She explained that the road map on the Strategic Approach to Pharmaceuticals in the Environment of the COM expresses what has to be investigated further. According to Ms Clayton, an impact assessment is needed for legally binding measures. Therefore, the COM first wants to publish the Strategic Approach.
- A participant from an NGO draw attention to the situation in China and India regarding the production of antibiotics and the high environmental concentrations of these compounds measured in these countries. The participant was worried that the COM had excluded the Good Manufacturing Practice (GMP) from the Strategic Approach. The participant asked the COM to include GMP on the proposal for implementation and to do an impact assessment, or to mention GMP indirectly. Prof. Lübbert, Karin Kadenbach and Jutta Klasen agreed that the GMP approach is necessary. DG Environment and DG Santé were of the opinion that GMP is a tool to prove that the production itself is safe, and that GMP needs to be installed by a singular country, but the problem of AMR is transboundary.
- A participant representing the WHO mentioned that when discussions at the WHO started on the topic of GMP in relation to the environment this same problem came up. However, the WHO stated that they need assistance in the topic of antimicrobial resistance in the environment. Therefore the WHO askes the EU to try whatever they can do on the topic, and to step up somewhat the efforts in regard to GMP, because the EU has a strong voice in the world. The WHO further argued that 12% of the waste water in the world is directly discharged and that 60% of the population in the world is not connected to any waste water treatment system. In regard to the environment, the participant stated that the EU has to recognize that the situation in the EU is not comparable to that of the rest of the world. However, treatment of waste water as such should still be addressed on a global scale.
- In the opinion of a representative of a regulator, GMP only requires a small adjustment to include environmental issues. According to the regulator, this was the conclusion reached by a lawyer providing legal analysis. In this respect the regulator pointed out that the EU also signed the UN 2030 Sustainable Development Goals, and that the EU therefore needs to step up. On the topic of GMP, a representative from industry argued that action is needed but that the importance of the situation in India and China (and not in Europe) has to be kept in mind.
- A representative of an NGO mentioned that EFSA and EMA already set clear targets to reduce the use of antibiotics and prevent the spread of resistances in animals. He highlighted that treatment with reserve antibiotics is very important for humans and they should therefore not be used in livestock farming. The NGO representative highlighted that antimicrobial resistance against e.g. colistin is increasing. The Commission answered that this is only one target, but that the differ-

ences in the Member States could make things different on the ground. In this respect a representative from the WHO highlighted that the WHO already recommends that misuse of reserve antibiotics should be prevented, and asked the COM why they do not pick up these recommendations in the EU approaches.

- In reaction to this, Prof. Lübbert raised the question why it is still possible for veterinarians to treat a high share of an animal herd when only one or a few animals are sick. Mr Perez from DG Santé agreed that pharmacist and veterinarian should work closer together. A representative from the association of the veterinary pharmaceutical industry clarified that antibiotics cannot be used as growth promotors, which is already forbidden, and that in Germany for example only a few antibiotics show an increase in use, which is minor in size. In accordance to this person, this is shown by the data from the German Federal Office for Consumer Protection and Food Safety. The Office has published data which demonstrates that the overall volumes of antibiotics being dispensed is decreasing.
- A person from the industry pointed out that a lot of work is done at the EMA by several antimicrobial resistance experts. They stated that the dispensation of antibiotics in humans and animals has to be seen as two different situations. They recommended to implement simplistic measures for veterinarians.
- A representative from the association of the veterinary pharmaceutical industry suggested to increase awareness for travellers who travel to specific regions with high antimicrobial resistant prevalence. Prof. Lübbert replied that it is not realistic to make a restriction on travel. He pointed out that surveillance might be a more useful tool to combat antimicrobial resistance. According to him, more transparency on human use and for the veterinary sector is urgently needed.
- Mr Perez from DG Santé stated that citizens' behaviour should be included among implemented measures, and that awareness is very important. In regard to this it should be clear who is prescribing what. A link should be made between the prescriptions for antibiotics with the antibiotic resistance found in the environment. In the opinion of Mr Perez, a survey is needed on this issue. Training should take place in different countries. In regard to the import of antimicrobial resistance from abroad, he highlighted that surveillance is also needed in countries like China and India, not only in the EU. He mentioned the potential of stewardship programs such as those existing in the Netherlands and Sweden, and suggested that they are needed globally. In Mr Perez's view, there should be a change of the veterinary practice; however, changes in consumer behaviour might be more effective in his opinion.
- Ms Kadenbach stated that one month ago the EU Parliament reached agreement on the new VMP regulation. It forbids metaphylaxis; prophylaxis is only allowed when needed. She proclaimed that animals should receive the best treatment possible, but that she does not understand why such high dosages are needed. Ms Kadenbach pointed out that for instance poultry and chicken are fed for almost two weeks on antibiotics in order to guarantee cheap production. She asked the audience if they want an agriculture that needs such high amounts of antibiotics and how typical agricultural practice can be financed without causing environmental impact. Ms Kadenbach stated that beside a focus on humans and the environment, focus should also be placed on agricultural practice.
- In regard to this point, a participant from FAO mentioned that the negotiations on the regulation of veterinary medicinal practice addresses the use in animals. The person stated further that the EU is one of very few places in the world where harmonised approaches are used. The person concluded that if it this should be taken up in the rest of the world there is a lot of work to be done. Therefore the participant from FAO highlighted the importance of spreading existing best practice to other regions.

- A participant from the healthcare and research sector highlighted the industry alliance on antimicrobial resistance on the human health side. The participant said that ECDC figures speak for themselves, because antimicrobial resistance is still increasing. The participant asked the Commission, regarding the AMR action plan monitoring process in the EU, what was assessed to be the most successful measure and what was deemed to not work that well. The participant also wanted to know which challenges the Commission faces. To the EU Parliament, the participant pointed out the discussed threshold values for water discharge that were also mentioned in the work performed by Joakim Larsson, published in September 2018.
- One participant asked about the effects of chemicals from mixtures and the possible co-selection and cross resistances that might occur. The person asked if there is a possible legal basis to address this issue and if the existing criteria are suitable to address mixtures. Jutta Klasen answered this point, referring to existing criteria for biocides and pesticides.
- Mr Perez from DG Santé confirmed that the One Health Antimicrobial Action Plan is very important but not sufficient to combat antimicrobial resistance. He stated that good results already exist, but that everyone has to do more.

4 World Café discussions

4.1 World Café Table 1 – Options for communication and authorisation

The discussions at Table 1 focused on the options for communication and authorisation identified in the UBA Background Paper "Antibiotics and Antibiotic Resistances in the Environment: Background, Challenges and Options for Action".[2] In particular, the options presented as example measures were:

The use of antibiotics should be limited to the medically necessary level. For this purpose, improved awareness and information is required in the area of human and veterinary medicine *(UBA report code: I.1.; Effectiveness horizon: short term; Target group/level: doctor / veterinarian)*: To minimize antibiotics and antibiotic resistances that enter the environment, antibiotics should be taken with caution. Consistent hygiene measures and the professional use of antibiotics for humans and animals should therefore be key for awareness rising.

Doctors, pharmacists, veterinarians and farmers must be informed and trained on the topic of antibiotics in the environment in a target-group-specific way *(UBA report code: II.1; Effectiveness horizon: short-medium term; Target group/level: EU, national, regional)*: A comprehensive programme of information and training on antibiotics and the environment should contribute to informing specific target groups. In addition to an EU strategic approach, at the national level it is necessary to clarify how the relevant groups which prescribe and use antibiotics can be informed and trained on a targeted basis.

Campaigns on the correct disposal of antibiotic residues are necessary *(UBA report code: II.2; Effectiveness horizon: short-medium term; Target group/level: EU, national, regional)*: Information on the correct and environmentally sound use and disposal of antibiotics should be available for all healthcare participants as well as for farmers, veterinarians and patients. Campaigns should highlight the role of the environment as a "reservoir" for the input of antibiotic substances and the resulting consequences.

[2] The English version of the report can be found under the following link: https://www.umweltbundesamt.de/publikationen/antibiotics-antibiotic-resistances-in-the
A German version is available under the link: https://www.umweltbundesamt.de/publikationen/antibiotika-antibiotikaresistenzen-in-der-umwelt

Develop and implement assessment methods and criteria for antibiotics and antibiotic resistances *(UBA report code: III.1; Effectiveness horizon: medium term; Target group/level: EU)*: It is necessary to develop assessment methods and criteria which should be included in the guidelines for the environmental risk assessment of human and veterinary medicinal products.

Develop and implement a risk assessment for the occurrence of resistances in the scope of the post-authorisation control of antibiotics and antibiotic resistances in human and veterinary medicinal products *(UBA report code: III.2.; Effectiveness horizon: medium term; Target group/level: EU)*: Measurements of antibiotics and antibiotic resistances are required in the scope of the post-authorisation control. It is equally necessary to develop standardised test methods as well as risk assessment approaches to document the extent of the emissions.

Publish environmental data from the authorisation of antibiotics *(UBA report code: III.3.; Effectiveness horizon: short-medium term; Target group/level: EU)*: The environmental risk assessment for the authorisation provides valuable substance-related information which can be used for the deriving of environmental quality standards as regards the legislation on water. Such data should be collated in a publicly accessible, Europe-wide database.

Include environmental considerations in the risk-benefit analysis for the authorisation of antibiotics for human medicine *(UBA report code: III.5.; Effectiveness horizon: short-medium term; Target group/level: EU)*: As is the case with VMPs, risks to the environment should be considered in a risk-benefit analysis, so that the risk of of antibiotic resistances is taken into account during the authorisation, and possible risks can be adequately documented in the post-authorisation control (pharmacovigilance).

The discussion focused on the following aspects of these action fields (as in other World Café tables):

- Benefits (Short term, Medium term, Long term)?
- Feasibility?
- Barriers?
- Preconditions?
- Synergies?
- Who plays which role in uptake?
- Further comments?

Two of the three World Café groups discussed the options addressing **communication.** Regarding the benefits of these measures, both groups stated that communication in general can be seen as having a high impact on reducing the input of antibiotics and the spread of antimicrobial resistance in the environment.

More specifically, both groups mentioned that all players in the prescription and usage chain of antibiotics (doctors, pharmacists, patients, veterinarian, farmers) should be included in the communication measures. Education, training, information campaigns, etc. should be developed as target-specific communication.

Benchmarking of antibiotic usage and prescription should be considered (e.g. why does a hospital use more antibiotics for the same treatment as another?). Experience exchange can be one way forward. Campaigns on the disposal of unused antibiotics were also mentioned by both groups as an important measure to reduce antibiotic residues in the environment.

The groups agreed that all measures regarding communication can be implemented on a short term basis. The feasibility for these measures in the opinion of the two groups is very high, with very easy

implementation. Barriers for the communication measures were seen in the scepticism of patients, who sometimes expect a prescription of an antibiotic when they visit a doctor.

The recommendation of doctors to live healthier so as to prevent diseases is not the first thing patients will want to hear when seeking help. One participant mentioned that the conditions for a better communication can be realised through the actions of supportive politics.

In terms of preconditions, both groups mentioned that it is important to clearly identify and to know your audience. One group highlighted that group-specific communication is important for a successful transfer of knowledge and recommendations.

On the topic of synergies, the groups discussed that measures on communication can be mentioned in the One Health Action Plan – and in the WHO approach.

For both groups it was clear that everybody who plays a role in the prescription, distribution and usage of antibiotics needs to change their behaviour. Therefore communication can start on local, national and European level. However, communication to patients should make sure that there is no risk of underdosage of a certain antibiotic.

Further, it was discussed in the groups that constant communication is necessary to reduce antibiotics and antimicrobial resistance in the environment. It was agreed that it is easier to reduce the input of antibiotics and AMR at source than to have an end-of-pipe solution. A majority was also of the opinion that there should be more transparency in the prescription of antibiotics. Communication on prevention and hygienic aspects (e.g. separating humans from the pathogen source) were also mentioned. In addition, communication addressing disposal should be examined and improved.

Measures in regard to the **authorisation** of antibiotics were only discussed by one group. The benefits of measures implemented in the authorisation of antibiotics were assessed by the group as high when it comes to their potential to reduce antibiotics and antibiotic resistance in the environment.

The group discussed that an environmental risk assessment on a substance-based level is a way forward regarding authorization, because residues and resistances found in the environment cannot be traced back to a single product but only to a substance used in several different products on the market (and often used for both humans and animals).

The other main measure discussed was the development and implementation of a method for assessing an antibiotic's potency to develop antimicrobial resistance in the environment. Such methods already exist for the development of AMR in animals and humans.

In this respect, further discussions ensued on how to use the information of such "potency-AMR-development" studies in the authorisation process of antibiotics. The opinion of the majority of the participants of this group was that such information has to be considered in the overall benefit-risk analysis and should have consequences for the authorization of veterinary medicinal products, but not for the authorization of human medicinal products. However, it was suggested that for human medicinal products considered to have the potency to develop AMR in the environment, post-market measures (e.g. monitoring, surveillance, etc.) should be required.

The time horizon for the implementation of the discussed measures was considered to be from medium to long term.

A barrier for the measure's implementation was seen in the current, product-based authorisation. Due to the lack of transparency of end-point reporting and because of the issue of legacy products, the information available for an antibiotic substance is often not complete.

Preconditions mentioned by attendees was method development to assess the potential development of antimicrobial resistance in the environment, which was seen as urgently needed, and the development of a guideline that defines the consequences or actions that the obtained information will trigger.

Because the authorisation of human medicinal antibiotic products and veterinary medicinal antibiotic products are already implemented in the corresponding legislation, synergies for a substance-based approach for the assessment were seen in the regulation of e.g. biocides and REACH. It was also discussed that the discharge of antibiotics should be communicated.

The role of different actor groups in uptake of measures was not addressed by the group, but because the authorisation of antibiotics both in the human health as well as in the veterinary sector is related to EU legislation, the actors and their roles are already predetermined.

It was highlighted that substance-related assessment in regard to authorisation is difficult when what is required is a management plan for a reduction of antibiotics. For the risk management of antibiotics and antimicrobial resistance in the environment, a substance-related assessment would be an advantage.

4.2 World Café Table 2 – Options regarding environmental waters and waste water treatment

The discussions at Table 2 focused on the options on options regarding environmental waters and waste water treatment identified in the UBA Background Paper "Antibiotics and Antibiotic Resistances in the Environment: Background, Challenges and Options for Action". In particular, the options presented as example measures were:

Identify hotspots for the discharge of antibiotics and antibiotic resistances, develop monitoring guidelines to better monitor these discharges *(UBA report code: IV.1 + IV.2; Effectiveness horizon: medium term; Target group/level: EU, national)*: A screening of the relevance of entry paths should take place so as to identify "hotspots". In addition to municipal waste water, the focus should be on healthcare institutions (hospitals, care homes), airports, and slaughterhouses. Systematic monitoring of antibiotic substances, ARB and ARG must occur in order to forecast the actual scope of the environment as a reservoir for resistances, for which guidelines are urgently required.

Address antibiotic residues and antibiotic resistances adequately in the statutory waste water provisions, extend assessment criteria for treatment performance and quality of effluent *(UBA report code: IV.3 + IV.4.; Effectiveness horizon: medium term, long term; Target group/level: EU, national)*: To date there are no specific requirements in the UWWTD concerning medicinal products and/or antibiotics discharged in municipal waste water. The quality of effluent from WWTPs is also insufficiently examined, and specific requirements concerning individual antibiotic substances are yet to be determined. Current assessment criteria of waste water treatment plants' performance should be extended with new chemical, eco-toxicological and microbiological parameters.

Improve the technology at waste water treatment plants *(UBA report code: IV.5., Effectiveness horizon: medium term, long term; Target group/level: EU, national)*: Municipal waste water treatment plants are currently not configured for the complete elimination of poorly biodegradable compounds such as certain antibiotics, nor for a sufficient reduction of pathogens or AMR. UBA therefore recommends introducing more advanced treatment of waste water at large-scale treatment plants (size category 5, ca. 50 % of Germany's waste water) and smaller treatment plants which discharge into waters with sensitive uses (e.g. drinking water, bathing).

Compile production locations and examine their emissions; revise reference documents on BAT for the production of organic fine chemicals and update them regarding emissions from

the production of antibiotics *(UBA report code: IV.6 + IV.7.; Effectiveness horizon: medium term; Target group/level: International, EU)*: At the European level, the environmental requirements concerning the production of medicinal products are governed by the IE Directive. In the pending reviews of the statutory provisions at the EU and national level, the requirement should be taken up that antibiotic substances and antibiotic resistances in production facilities' waste water should be measured and documented. Production locations should be listed, and a systematic monitoring of the waste water should be carried out.

Implement environmental considerations in the "Good Manufacturing Practice" requirements for the production of antibiotics and in trade agreements *(UBA report code: IV.8;, Effectiveness horizon: medium term; Target group/level: EU)*: Production of antibiotic substances for Europe primarily takes place in Asia. Emissions of antibiotics and antibiotic resistances during production of active substances as well as through the "formulation" of medicinal end products in the EU and third countries should therefore be measured and reduced as required. Emissions should also be incorporated in the guidelines regarding GMP and be taken into account in trade agreements with third countries.

Include antibiotics and antibiotic resistances in the Water Framework Directive, take antibiotic resistances into account in the deriving of environmental quality standards *(UBA report code: V.2 + V.3.; Effectiveness horizon: medium term; Target group/level: EU, national)*: Antibiotic substances azithromycin, clarithromycin and erythromycin are at present measured in the scope of the WFD's watch list. However, no overview of antibiotic resistances in waters has been made available. The list of "priority substances" should be updated so that relevant substances can be measured, environmental quality standards set, and their concentrations be reduced. When deriving environmental quality standards for antibiotics, their ability to trigger resistances should be taken into account.

Reduce the input of antibiotic resistances into surface and bathing waters, e. g. through the widening of riparian strips and the designation of water protection zones *(UBA report code: V.4.; Effectiveness horizon: short-medium term; Target group/level: regional, municipal):* The input of resistances and resistance genes into water which is attributable to human activity, particularly livestock keeping, can be reduced at the local level through the widening of riparian strips, which prevents run-off and drifting into waters from the application of slurry. A consistent designation of water protection zones at the regional level is also a possibility.

Introduce a threshold value for antibiotics in the legislation concerning groundwater *(UBA report code: V.5.; Effectiveness horizon: medium term; Target group/level: EU, national):* For precautionary reasons, UBA recommends introducing a threshold value at European and national level for antibiotics for groundwater equivalent to the limit values for plant protection products and biocides. In the event of exceedance, this would provide the statutory basis for the regular verification of groundwater and more advanced measures.

The discussion focused on the following aspects of these action fields (as in other World Café tables):

- Benefits (Short term, Medium term, Long term)?
- Feasibility?
- Barriers?
- Preconditions?
- Synergies?
- Who plays which role in uptake?
- Further comments?

The overall opinion of the three groups of participants was that the main focus of measures addressing environmental waters and waste waters should not be on end-of-pipe type of solutions, but on

measures addressing sources. In addition, the majority of participants would prefer to have both statutory measures and measures that are not legally binding. Examples provided were a mandatory risk assessment for antimicrobial resistance, monitoring of AMR in the environment, and the revision of the Good Manufacturing Practice (GMP). The three groups focused their attention on only a few of all the proposed measures.

One group identified the need to include antibiotics and antibiotic resistance in the Water Framework Directive (WFD), as well as taking antibiotic resistance into account in the establishment of environmental quality standards, as the most successful way to reduce antimicrobial resistance.

However, regarding the feasibility of this measure, the groups mentioned that there are few indicator species or parameters to measure resistance, that there is a lack of available data, and that resources are scarce. In this context a WHO representative mentioned the WHO had created an Expert Group called "AGESR Group" with the aim of identifying how to quantify antibiotic residues and antimicrobial resistance. The group should have developed results within one year. In this regard the ERICYCLE Project was also mentioned.

Barriers to implementing the uptake of antimicrobial resistance in the WFD were seen in the sampling methods and the accuracy of sampling results. To date, monitoring guidelines on how to measure these parameters in a harmonised way do not exist. One participant mentioned that at present 60% of samples taken have a high variability because of the lack of guidelines. One demand was the standardization of sampling and analysis technologies, which can be then used as a protocol for these actions. The majority of participants was of the opinion that it is necessary to include antimicrobial resistance in the environmental monitoring systems. In this regard it was mentioned in one group that measures should be implemented not only on the local or national level within the EU, but also on an international level.

Regarding the uptake of antibiotic substances in the WFD, one group held that it is clear that residues can be found in the environment and that thresholds are urgently needed for antibiotic residues. However, more effort than just monitoring would be required, and there should be a focus on introducing instruments to reduce the release of antibiotics into the environment (prevention). In this regard the unnecessary use of antibiotics was discussed.

Another barrier identified by two of the three groups was the question of if the polluter-pays principle should play a role in the reduction of antibiotic residues and antimicrobial resistance. This was seen in the context of the lack of waste water treatment plants (WWTPs) in some areas, and the need for best available technology of WWTPs at emission hotspots. It was discussed that determining the adequate technology is not easy, and that there are differences between a municipal authority's waste water and that of a hospital. On the topic of identification of hotspots the HYREKA project was mentioned, which addresses the best available technologies and the set-up of WWTPs. However one aspect highlighted in the discussions was the high cost of a good and effective waste water treatment technique.

In this context, emissions derived from the manufacturing process were discussed by one group. It was mentioned that manufacturing sites should do a better job at analysing their emissions in view of a more efficient source control. A participant mentioned that GMP is dealing with very specific areas and that it has to be implemented on a global scale, because only 5% of the antibiotics are produced in the EU. In this context it was pointed out that it could be difficult for smaller factories to deal with GMP requirements due to which the market could become closed for some production sites, and that the revision of the GMP system could thus have an effect on trade. However, one group raised the question whether we know where the manufacturing sites are located.

Attendees of two groups pointed out that arrangements should be in place when it comes to the identification of hotspots. The need for an exhaustive connection with WWTPs and for the improvement of treatment technology so that they address antimicrobial substances and their metabolites was also seen by one group as a measure. One precondition for an effective measure identified was guidelines

for technologies and standardisation of measurement methods, in combination with defined threshold values. Most participants of the three groups saw this point as an important precondition.

Synergies with existing legislation were mainly seen on two aspects. An opinion expressed by most participants in the three groups was that the Water Framework Directive should be amended and that waste water treatment technology should be improved at hotspots. One group also discussed the Urban Waste Water directive as having synergies with the issue of antibiotics and antibiotic resistance in the environment.

The groups discussed different actors who might play a role in measure uptake. Several attendees see the pharmaceutical industry as the responsible actor, with Member States carrying the responsibility of identifying hotspots.

4.3 World Café Table 3 – Options in practices related to soil and agriculture

The discussions at Table 3 focused on the options on practices related to soil and agriculture identified in the UBA Background Paper "Antibiotics and Antibiotic Resistances in the Environment: Background, Challenges and Options for Action". In particular, the options presented as example measures were:

A species-appropriate animal husbandry can help prevent illnesses. Pharmaceutical forms for application should be adapted to reduce the residues of antibiotics in excreta *(UBA report code: I.2.; Effectiveness horizon: short term; Target group/level: farmer / veterinarian):* A risk-oriented, preventive form of health management is necessary in livestock farming, as antibiotics which are not used in the first place cannot contaminate the environment. Preventive measures include husbandry conditions which prevent illnesses, strengthening of animals' immune systems, and systematic monitoring of their health. Input reductions can be achieved by choosing the appropriate pharmaceutical form for the application (e.g. changing from oral to injection).

Prohibit the application of sewage sludge onto soil and use sewage sludge for the recovery of phosphorous *(UBA report code: VI.1.; Effectiveness horizon: medium term; Target group/level: national, EU):* In future, the direct use of sewage sludge and of sewage-sludge recyclates for fertilising is to be prohibited in Germany for large-scale waste water treatment plants (> 50,000 PE). Smaller treatment plants can continue to use sewage sludge and its recyclates for soil-related purposes. Detailed assessments of the risk of sewage sludge use as fertiliser should therefore be carried out. In the long term, there should be efforts to completely withdraw from agricultural use of sewage sludge on the national and EU level.

Needs-based fertilisation – demand assessments for fertilisers on the basis of in-house analyses (soil analysis, nutrient content of farm fertiliser) *(UBA report code: VI.2.; Effectiveness horizon: medium term; Target group/level: EU, national):* Measures to reduce the quantities of agricultural fertilisers (possibly required in updates of MSs' fertiliser legislation related to the Nitrates Directive) indirectly reduce antibiotics in the environment. Reducing fertiliser use requires an increase in their use effectiveness. For this purpose, a realistic and location-adapted needs assessment for fertiliser is necessary, making use for instance of in-house values of soil analyses and measurements of the nutrient content of farm fertiliser, instead of standard values that are less-exact.

Introduce compulsory documentation of antibiotics used in livestock and the co-selectors of zinc and copper used as animal feed *(UBA report code: VI.3.; Effectiveness horizon: short term; Target group/level: EU, national):* Since occurrence and dissemination of resistances is to be expected even with low concentrations of antibiotics and is strengthened by zinc and copper, it is important to know the antibiotic substances and the quantities of zinc and copper present in the slurry. The documenta-

tion of these quantities can be linked with the compulsory documentation on antibiotic use of antibiotics in livestock farming without requirements for further analysis, and is thus possible with a relatively low level of effort.

In the form of slurry delivery notes, pass on information concerning the production and transport of slurry and its application on the soil *(UBA report code: VI.4.; Effectiveness horizon: medium term; Target group/level: EU, national):* The quantity of antibiotics and the substances used, as well as the zinc and copper contents, could be included together with the other required slurry parameters (including the N and P content) in a slurry delivery note, and transferred throughout the life cycle of the slurry up until its application on the soil. This would allow for a more specific monitoring of those farm fertilisers that are contaminated with antibiotics and which are used by several different farmers.

Examine the dissemination of antibiotic residues and antibiotic-resistant bacteria through sampling at selected arable farmland locations, and define precautionary and possible limit values for antibiotics as well as zinc and copper in the soil *(UBA report code: VII.1.; Effectiveness horizon: medium term; Target group/level: national):* The current data basis is insufficient for deriving EQS or precautionary values for antibiotic residues in soil. Selected locations subjected to the regular application of sludge and slurry at which known co-factors for the forming of resistances occur should be examined. In a next step, suitable measures could be derived and implemented. Precautionary values for the concentrations of antibiotics in slurry should be developed in order to prevent an "accumulation" of persistent antibiotic residues in soil. Input of zinc and copper (used as feed additives) into soil also enforces the selection pressure and spread of antibiotic resistances; as they remain in soil for a very long time, upper limits for their application should be defined so as to prevent their accumulation.

The discussion focused on the following aspects of these action fields (as in other World Café tables):

- Benefits (Short term, Medium term, Long term)?
- Feasibility?
- Barriers?
- Preconditions?
- Synergies?
- Who plays which role in uptake?
- Further comments?

Firstly, it should be noted that the area of work of the vast majority of workshop participants is related to animal healthcare and its regulation; in consequence, the discussions on options related to agriculture and soil tended to focus on measures in the field of animal husbandry rather than on measures related to e.g. crop fertilisation.

Group participants were of the opinion that the potential of this group of measures to reduce the input of antibiotics and antibiotic resistance in the environment was high. In particular, they highlighted the very high potential of changes in animal husbandry to mitigate the environmental input of antibiotics. One group counted among these measures' benefits the very significant savings for national health services due to reduced antibiotic resistance and its impacts on human health.

Workshop attendees saw this type of measures as feasible. References were made to the Scandinavian countries, where documentation requirements such as those of measures IV.3 and IV.4 have already been implemented for a number of years. Benchmarks were suggested as an approach that can do justice to the different conditions and potential of measures in the farming of cattle, pigs, poultry, etc. The conformity with this kind of benchmarks could be expressed in a 'traffic light' system, according to one

group. The impact of related measures, such as adapting animal nutrition to improve herd health, was considered significant.

Regarding barriers to the implementation of this group of measures, opinions differed regarding the cost of measures related to documentation. Whereas some highlighted the enormous amounts of daily produced slurry for which documentation would be required (i.e. generating high costs), others emphasised the similarity of these requirements with already existing ones (implying that no major costs would be incurred in expanding documentation requirements). The latter participants saw the barriers for this type of measures rather in the knowledge gaps on the topic, including on the question of precautionary values for antibiotics in soil (measure VII.1). Some participants highlighted that farmers are strongly averse to documentation requirements ("farmers hate paperwork"), and that this kind of measures does not enjoy huge support among this actor group.

On the topic of preconditions for successful implementation of such measures, one group highlighted the need for strong political interest so as to be able to implement these requirements. However, implementation should not be "against" farmers, but would rather require their early and intensive involvement, so as to reach a result that reflects as much as possible their requirements and is compatible with their operating procedures. On the side of consumers, participants highlighted the importance of their being willing to pay for the price difference that changes to animal production in Europe would entail. Care should be taken so as to avoid the possibility of undesirable behaviour, such as the new rules being "gamed", i.e. that compliance is only achieved on paper.

The World Café groups identified synergies with existing policy frameworks as well as with upcoming policy issues and social trends. Significant synergies of these types of measures with the Common Agricultural Policy were highlighted, as well as with consumer reduction in meat consumption, which in turn has positive impacts on climate change mitigation objectives (as reduction of livestock production would help reduce agriculture's greenhouse gas emissions). Not all these measures would have to be costly, participants highlighted, as they saw inexpensive options with potential for reducing antibiotic input and resistance as well as addressing other policy areas. They also highlighted the strong synergies that could be achieved in the field of communication and awareness-raising on the topic; jointly addressing antibiotic resistance with topics such as meat consumption and climate change would greatly help the prominence of the issue of antibiotic resistance. On the consumer side, another important topic that would have significant synergies with antibiotic resistance would be animal welfare. For farmers and regulators, strong synergies would exist between the topic of antibiotics in the environment and farm-level biosecurity.

The discussions on the roles of actors in the uptake of these measures coincided in putting the emphasis on the political level as the one with the main responsibility. The most significant role in implementation was located at the Member States' level; this level would be the relevant one due to the country-specific aspects of animal production in MSs. One group highlighted the importance of the EU level for providing the overarching rules for establishing measures of this type in MSs. Consumers, on the other hand, would have the responsibility of making their voices heard when it comes to advocating for changes to the current form of livestock production.

Annex I – Workshop Agenda

Workshop
"Act Now – Antibiotics and Antibiotic Resistance in the Environment"

Date: November 7, 2018 – 10:30 to 15:30

Venue: Permanent Representation of the Federal Republic of Germany to the European Union, Jacques de Lalaingstraat 8-14, 1040 – Brussels

Programme	
10:00 – 10:30	**Arrival and registration of participants, Welcome Coffee**
10:30 – 10:40	**Welcome** *Jutta Klasen*, German Environment Agency (UBA) *Viktor Szontagh*, Permanent Representation of Austria to the EU
10:40 – 10:50	**Workshop introduction** *Rodrigo Vidaurre*, Ecologic Institute
10:50 – 11:10	**Multi-drug resistance as a growing global problem and its impacts in Germany** *Prof. Christoph Lübbert*, Department of Infectious Diseases and Tropical Medicine, University Hospital Leipzig
11:10 – 11:20	**The EU Commission's Strategic Approach to Pharmaceuticals in the Environment** *Helen Clayton*, DG Environment
11:20 – 11:30	**The European One Health Action Plan against Antimicrobial Resistance** *Aurélien Perez*, DG Health and Food Safety
11:30 – 11:40	**Environment in the One Health Action Plan of the European Parliament** *Karin Kadenbach*, MEP, Rapporteur in the European Parliament on the EU's One Health Action Plan against Antimicrobial Resistance
11:40 – 11:55	**Options to minimise antibiotics and antibiotic resistance in the environment** *Jutta Klasen*, Head of Chemical Safety Division, German Environment Agency (UBA)
11:55 – 12:45	**Q&A and Panel Discussion #1: Potential of and synergies between the EU initiatives from the perspective of antibiotics and antimicrobial resistance** *Christoph Lübbert, Helen Clayton, Karin Kadenbach, Jutta Klasen*
12:45 – 13:45	**Lunch**
13:45 – 13:50	**Introduction to afternoon session** *Rodrigo Vidaurre*, Ecologic Institute
13:15 – 15:10	**Group work (World Café) on possible courses of action:** **Actor responsibilities, barriers and synergies in measure implementation**
15:10 – 15:30	**Panel discussion #2: Reactions to World Café findings** *Christoph Lübbert, Helen Clayton, Jutta Klasen*
15:30	**Closing remarks and end of workshop**

Annex II – List of Participants

Workshop: "Act now – Antibiotics and Antibiotic resistance in the environment"

November 7, 2018 | Brussels

List of Participants

Surname	*Name*	*Institution*
Adler	Nicole	German Environment Agency
Aldinger	Georg	Representation of the State of North Rhine-Westphalia to the European Union
Andrei	Daniela-Valeria	Permanent Representation of Romania to the EU
Baars	Christian	Norddeutscher Rundfunk (NDR)
Benning	Reinhild	Germanwatch
Brozmanova	Maria	Permanent Representation of the Slovak Republic to the EU
Buchner	Klaus	European Parliament
Carapeto García	Ricardo	Spanish Medicines Agency
Cassarino	Georgia	GlaxoSmithKline
Clayton	Helen	European Commission
Eklund	Gunilla	Food and Agriculture Organization of the United Nations (FAO)
Goret	Michel	Federal Agency for Medicines and Health Products
Gripp	Tamara	PAN Germany (Pestizid Aktions-Netzwerk e.V.)
Haro	Amparo	Spanish Medicines Agency
Harpur	Matthew	UK Permanent Representation to the EU
Heberer	Charly	European Parliament
Hodan	Martin	European Parliament
Hughes	Eilyr	Menter a Busnes

Surname	*Name*	*Institution*
John	David	AnimalhealthEurope
Juch	Veronika	Food and Agriculture Organization (FAO)
Kadenbach	Karin	European Parliament
Klasen	Jutta	German Environment Agency
Kmetic	Klavdija	Association of European Self-Medication Industry (AESGP)
Koeper	Lydia	Federal Office of Consumer Protection and Food Safety (BVL)
Küster	Anette	German Environment Agency
Lobosco	Hanna	Ministry of Health and Social Affairs
Lübbert	Christoph	Leipzig University Hospital, Germany
Lührs	Maraike	Bundesverband der Energie- und Wasserwirtschaft e.V. (BDEW.e.V).
Maghear	Adela	Health Care Without Harm Europe (HCWH Europe)
Milkowska	Maja	Health Care Without Harm
Müller	Susanne	Ecologic Institute
Neger	Ingrid	European Parliament
Ogawa	Misachi	Acumen Public Affairs
Perez	Aurélien	European Commission, DG Santé
Poetschke	Felix	German Environment Agency
Reichel	Angela	Pro Generika e.V.
Renwrantz	Leonie	Permanent Representation of Germany to the EU
Royston	Victoria	European Parliament
Salin	Kia	Swedish Medical Products Agency
Schreiber	Frank	Federal Institute for Materials Research and Testing (BAM)
Schwarz	Christine	Federal Office of Consumer Protection and Food Safety (BVL)
Seilnacht	Johannes	Ecologic Institute

Surname	*Name*	*Institution*
Sekidde	Serufusa	GlaxoSmithKlein (GSK)
Sigge	Claudia	Bundesverband für Tiergesundheit e.V.
Simon	Tony	Zoetis
Staicu	Stefan	Permanent Representation of Romania to the EU
Stapleton	Ken	Veterinary Medicines Directorate
Stelmaszyk	Lara	German Technical and Scientific Association for Gas and Water –Water Technology Centre (DVGW- Water Technology Centre)
Szontagh	Viktor	Permanent Representation of Austria to the EU
Turosz	Yoan	Permanent Representation of France to the EU
Urbancic	Nusa	Changing Markets Foundation
Vidaurre	Rodrigo	Ecologic Institute
Wallin	Maria	Swedish Ministry for the Environment and Energy
Wester	Astrid Louise	World Health Organization
Ziegelmann	Antina	Federal Ministry of Health