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Economic Cooperation

Workshop Report – Coordinated Research Initiative for the Implementation of Antimicrobial Resistance Control Strategies

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Sub-Committee on Standards and Conformance

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Executive Summary

The APEC Workshop on Coordinated Research Initiative for the Implementation of Antimicrobial Resistance Control Strategies was held on 28, 29 and 30 October 2015 in Santiago, Chile. Attendance at the Workshop includes speakers, experts, officials, representatives from APEC member economies, namely: Australia, Canada, Chile, People´s Republic of China, Indonesia, Malaysia, Mexico, New Zealand, Papua New Guinea, Peru, The Philippines, Thailand, The United States, Viet Nam and international organizations, corporations and associations in Food Safety in general, like PAHO and OIE..

The Workshop provided the opportunities for participants to share experiences, discuss and enhance awareness, skills and knowledge in the field of AMR (focused on bacterial antimicrobial resistance), as a worldwide emerging issue in public health; strengthen technical competence of APEC economies´ representatives working in the areas related with AMR. This objective wasaddressed by the lectures given by the invited experts who participated in the workshop; these experts provided APEC economies´ representatives with the tools to address this public health problem in order to work towards harmonized and standardized methodologies. To increase understanding of the control strategies to address the emergence and spread of AMR the workshop examined practices used by other economies in the region and international organizations. The workshop helped to build competency and capacity in AMR surveillance through knowledge transfer between APEC economies from those that have surveillance systems to those who are considering initiating programs.

Introduction

Food safety regulatory standards are a qualitative and reliable indicator of the ever changing dynamics of the domestic legislation each economy has regarding food safety.

The APEC Food Safety Cooperation Forum (FSCF) was formally established under the APEC Sub-Committee for Standards and Conformance (SCSC) where the APEC Leaders agreed to work together to build robust food safety systems that are consistent with the SPS and TBT Agreements of the WTO, to accelerate progress on harmonizing food standards with international standards (such as Codex, OIE, IPPC), improve public health and facilitate trade.

In support of APEC's 2014 Rank 1 priority of promoting regional economic integration via free and open trade and investment through standards, conformity assessment, technical regulation and regulatory cooperation, Chile obtained APEC funding to conduct a Workshop in antimicrobial resistance control strategies.

The focus was on Antimicrobial resistance (AMR) present in microbial strains isolated from animals, environment and food, in order to lay the foundations and economies' needs for establishing a Resistance Surveillance System in each economy in the short term. Economies with more experience in the subject and ongoing surveillance systems contributed expertise and training materials for the workshop. OIE and the WHO are key stakeholders of this initiative, considering the tripartite effort that FAO/OIE/WHO have made in order to develop a joint action plan on AMR. The Codex Alimentarius Commission Guidelines for Risk Analysis of Foodborne Antimicrobial Resistance was considered in the project implementation. The outcomes of this Workshop will be a capacity building training module on antimicrobial resistance for use by all APEC economies and this final report.

Workshop results

The following section provides a summary of the presentations given during the workshop.

Opening Remark

Claudio Ternecier, Undersecretary of Agriculture
Andres Culagovski, Head of APEC Department, DIRECON
Michel Leporati, Executive Secretary, ACHIPIA
Santiago Urcelay, Dean FAVET

Session 1: **Awareness**

The objective of this session was to enhance awareness, skills and knowledge in the field of AMR (focused on bacterial antimicrobial resistance), as a worldwide emerging issue in public health.

Participants included APEC Members from Chile, The United States, and Canada. It also featured the presentations from delegates from OIE, PAHO, FAO, , The Netherlands and Ireland.

Dr. Javiera Cornejo, Assistant Professor at the Faculty of Veterinary and Animal Sciences of the University of Chile (FAVET), presented a description of the objectives for APEC project "Coordinated Research Initiative for the Implementation of Antimicrobial Resistance Control Strategies". Since 1994 Bogor Leaders' Declaration underlines APEC's commitment to achieve sustainable and equitable growth and reduce economic disparities for the well-being of its people, by the decrease in the disparity of the approach presented by the different economies in facing a relevant problem to the regional, and worldwide public health. Balis declaration enhances the importance of the APEC economies engagement in capacity building efforts, and effective regional and global partnerships across the public and private sectors with the aim of addressing emerging infectious diseases, and strengthening public health systems; in alignment with the need to work on combating infectious diseases. According to the WHO, Antimicrobial resistance (AMR) has the potential to threaten health security, and damage trade and economies. It affects developing economies proportionally more than developed ones. So, this project supports the APEC need to reinforce economic cooperation in the Asia-Pacific region on the basis on equal partnership, shared responsibility, mutual respect, common interest, and common benefits, as stated in above mentioned declaration. On these topics, one issue of special concern for all the economies is the emergence of antimicrobial resistance (AMR), associated to food animal production.

WHO has implemented a number of initiatives in different regions in order to strengthen inter-sectoral coordination and surveillance of AMR. The WHO has formed the Advisory Group on Integrated Surveillance of AMR (AGISAR), to support these efforts.

OIE has developed activities aimed to combat AMR in Animals/Veterinary Sector activities. FAO/OIE/WHO Tripartite High level Coordinating Forum has defined AMR as one of 5 priority issues in need of a joint action plan and one common voice on the issue.

Currently, there are differences in how APEC economies are managing the issue of AMR. This is highlighted by the different approaches used for the design and implementation of resistance surveillance systems in each economy. This creates differences in standards and technical regulations, affecting open trade and the regional commercial flow of food. The lack of regional integration on this issue has the potential to impact the availability of safe food products for the population. In order for APEC to continue to facilitate free flow of traded food products, contributing to regional economic growth and integration of the economies, and support of food safety and food security practices in the region, APEC member economies must align and improve their systems for surveillance and monitoring of AMR in human, animals and environment.

The project objectives are to enhance awareness, skills and knowledge in the field of AMR, as a worldwide emerging issue in public health. Strengthen technical competence of APEC economies representatives working in the areas related with AMR. Increase understanding of the control strategies, emergence and spread of AMR. Build competency and capacity in AMR surveillance.

Dr. Patrick McDermott, Director of the National Antimicrobial Resistance Monitoring System at the FDA, presented a brief overview on the challenges and importance of developing integrated surveillance systems for antimicrobial resistance in the food supply. There are more than 100 antibacterial agents currently approved for use in clinical medicine, resistance has followed each new agent with varying time and frequency. The consequences of this problem are, more expensive/toxic drugs, additional diagnostic testing, extended illness or hospitalization, costs to patient/family, time from work, higher mortality, resistance genes remain a problem for the future the hospital/farm as reservoir.

Integrated surveillance of antimicrobial resistance in foodborne bacteria is the coordinated sampling and testing of bacteria from food animals, foods, and clinically ill humans; and the subsequent evaluation of antimicrobial resistance trends throughout the food production and supply chain using harmonized methods. Integrated antimicrobial resistance monitoring of foodborne pathogens is important to ensure the safety of the food supply and for public health policy. Sustainable integrated resistance surveillance is expensive, laborious and has many challenges, design and prioritization, collaboration across agencies, gathering and integrating information, understanding the implications of the data, publishing findings to different audiences in a timely manner, using the data to formulate sound public health policy. Because AMR is a global problem, there is a need for international harmonization of surveillance methods to ensure data comparability and cooperation and data sharing to limit global spread.

Dr. Enrique Perez, Senior Advisor Foodborne Diseases and Zoonosis at PAHO, described the WHO's effort to minimize the public health impact of antimicrobial resistance associated with the use of antimicrobials in food animals. Development of a AMR Global action plan to include intersectoral engagement and partnering, broad stakeholder participation, not a plan of action, but a commitment for action. The objectives of the action plan are to improve awareness and understanding of antimicrobial resistance through effective communication, education and training, strengthen the knowledge and evidence base through surveillance and research, reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures, optimize the use of antimicrobial medicines in human and animal health, develop the economic case for sustainable investment that takes account of the needs of all economies, and increase investment in new medicines, diagnostic tools, vaccines and other interventions.

To address AMR through integrated surveillance the WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance (AGISAR) was established in December 2008. It provides expert advice to WHO on containing food related antimicrobial resistance and promoting integrated surveillance of antimicrobial resistance and antimicrobial usage. AGISAR has participants from all 6 WHO regions, including representatives from FAO, OIE, ECDC. EFSA. They are physicians, microbiologists, veterinarians and epidemiologists.

In 2005 WHO developed a list of critically important antimicrobials, intended to help preserve the effectiveness of antimicrobials, its updated regularly and since 2009 its revisions are made by AGISAR. WHO has developed and applied criteria to rank antimicrobials according to their relative importance in human medicine. Clinicians, regulatory agencies, policy makers and other stakeholders can use this ranking when developing risk management strategies for the use of antimicrobials in food production animals. WHO also gives guidance on Integrated Surveillance of Antimicrobial Resistance through an important output of the 5 year strategic framework for AGISAR. It provides basic information that economies need to establish programs for integrated surveillance of resistance; it makes recommendations that facilitate global harmonization and data comparability.

Dr. Martin Minassian, Technical Assistant at OIE, gave a presentation of the OIE as an international standard setting body, describing standards and current actions in the field of AMR. Antimicrobial resistance is not a new phenomenon, but concerns are growing. Antimicrobial agents are essential to ensure human health, animal health and welfare, and food security. The human, animal and plant sectors have a shared responsibility to prevent or minimize the development of antimicrobial resistance by both human and non-human pathogens. This requires a tripartite agreement/vision from FAO, OIE and OMS to jointly address this issue. This includes a holistic and coordinated management across the animal, food and human sectors in different ecosystems and geographic locations and improved intersector collaboration where regulations of medicines are managed by different entities. This approach calls for the need for:

- International standards (to harmonize protocols and methodologies) to monitor AMR and antimicrobial usage.
- Surveillance data on AMR and antimicrobial usage to support AMR risk analysis.
- Technical capacity (for surveillance of AMR and antimicrobial usage and AMR risk analysis).
- Coordinated research on effectiveness of policies to achieve AMR risk reduction.
- R&D new drugs.
- Legislation on access to quality drugs and restricted use.
- Good governance of all sectors related to authorization and use of antimicrobials (lab expertise, international standards and legislation development and implementation, surveillance and monitoring).

The activities the OIE will carry out to tackle AMR were discussed, such as the update of guidelines and standards, recommendations for member economies, monitoring of antimicrobial quantities, a global database on the use of antimicrobials in animals and the list of antimicrobial agents of veterinary importance for which there are no or few alternatives. Among the veterinary critically important antimicrobial agents, some are also of critical importance for human health (third and fourth generation cephalosporins, and fluoroquinolones): Not to be used as preventive treatment in feed or water or in absence of clinical signs; not to be used as first line, unless justified and bacteriological test; extra label/ off label use must be limited and reserved for instances no alternatives are available.

To control antimicrobial use in animals we need: Support for developing economies to implement good governance aspects including veterinary legislation; quality veterinary services, including the private sector and laboratories; measures for controls on importation, production, distribution and use; involvement of all stakeholders; more risk assessment and banning of non-priority practices in animals. Awareness raising is needed at all levels, animal health and welfare must be sustained, food security and food safety must be ensured, veterinary supervision for animal use is a priority, no universal optimal solution for the delivery of antimicrobials at farm level worldwide, the well qualified veterinarian is crucial.

Ms. Deyanira Barrero, Regional Office for Latin America and the Caribbean at FAO, gave a presentation on the collaboration of the United Nations Food and Agriculture Organization (FAO) to tackle antimicrobial resistance. Importance of public policies and regional challenges.

Antimicrobial drugs play a critical role in the treatment of diseases; their use is essential to protect both human and animal health. However, antimicrobials are often misused for treatment and prevention of diseases in livestock sector, aquaculture as well as crop production. These actions are often associated with the potential risk of emergence and spread of antimicrobial resistant microorganisms. The very microbes that cause infections and disease are becoming resistant to antimicrobial drugs because of overuse, misuse and counterfeiting. The more these drugs are abused, the greater the likelihood that microbes will become resistant, thereby placing livestock and livelihoods at risk. Some economies lack laboratory facilities that can accurately identify resistant microorganisms: this impairs the ability to detect emergence of resistant microorganisms and take prompt actions. Similarly, there is insufficient new research into new diagnostics to detect resistant microorganisms, and vaccines for preventing and controlling infections. If this trend continues, the arsenals of tools to combat resistant microorganism will soon be depleted.

FAO plays a key role in supporting government, producers, traders and other stakeholders to adopt measures to minimize the use of antimicrobials and to prevent the development of antimicrobial resistance. FAO works on antimicrobial resistance with its international partners in the Tripartite (a collaboration between FAO, WHO and OIE) and also with other partners, as appropriate. FAO calls for a "One health" and "food chain" approach and is addressing Antimicrobial Resistance as a cross-sectoral issue because antimicrobials can spread through our food; are widely used in aquaculture and livestock production; are used in crop culture -more specifically antifungicides. To guard against antimicrobial resistance and as part of overall efforts to reduce hunger, FAO helps economies develop and promote:

- Good hygiene practices to control the spread of resistance through food.
- Attention to risk of antimicrobial resistance by Codex Alimentarius.
- Efficient livestock husbandry for healthier, more productive animals.
- Guidelines for prudent use of antimicrobials in aquaculture.
- Good animal health and management practices including improved biosecurity and use of vaccines instead of antimicrobial drugs.
- Policies and capacities for responsible use of antimicrobials.
- Health management approaches that recognize the links between animals, humans and ecosystems.

These measures help slow down the development and expansion of resistance to essential veterinary drugs.

There is a joint FAO/WHO food standards program, the Codex Alimentarius Commission. The major achievements of the Commission are the adoption of Code of Practice to Minimize and Contain Antimicrobial Resistance (CAC/RCP 61-2005), developed by CCRVDF; and the adoption of Guidelines on Risk Analysis of Foodborne Antimicrobial Resistance (CAC/GL 77-2011), developed by the TFAMR.

The FAO and animal feed industry 10 years old formal collaboration is now fully mature and takes up the challenge of addressing issues which are critical if the safety and sustainability of feed and food are to be ensured. FAO's commitment is to:

- Strengthen domestic and international interdisciplinary cooperation and developing holistic strategies and action plans.
- Improve regulatory frameworks based on internationally agreed principles and standards (Codex, OIE).
- Reduce the need for antimicrobials in animal husbandry, by improving animal health disease prevention and good practices along the chain.
- Strengthen food and human surveillance systems for AMR and the quantities of all antimicrobials being used at the domestic level.
- Raise awareness (among veterinarians, value chain actors including producers and the public) about AMR.
- Develop appropriate policies/guidance on the prudent and responsible use of antimicrobials in animal husbandry.
- Support research to generate data on the prevalence and trends in AMR, as well as supporting risk assessment, risk management and risk communication in the AMR area.

The prudent use of antimicrobials in livestock and aquaculture sector is essential in light of the increased demand for animal proteins by a rapidly growing world population expected to exceed 9.6 billion by 2050. Intensifying production mean additional challenges in disease management and even higher potential for increased antimicrobial resistance. Antimicrobial resistance can be tackled by working closely with veterinarians, farmers, feed and food producers and food safety professionals, to support best animal health and production practices, which underpin the prudent use of antimicrobials. For all these reasons, concerted global action is required to deal with AMR.

Dr. Rebecca Irwin, Director of the Canadian Integrated Program for Antimicrobial Resistance Surveillance Division of the Public Health Agency of Canada, presented a brief overview on the development of the Codex Guidelines For Risk Analysis of Foodborne Antimicrobial Resistance. The 29th session of the Codex Commission in 2006 decided to establish an intergovernmental task force on AMR. The taskforce led by South Korea was given a mandate to draft guidelines to assess the risks to human health associated with the presence in food and feed (including aquaculture), and the transmission through food and feed of AMR microorganisms and determinants, and to develop appropriate risk management measures. They met 4 times in Korea from 2007 to 2011 in which they drafted and then consolidated various documents into final guidelines.

The scope of the guidelines considered all non-human use of antimicrobials including those used in veterinary medicine, plants and food processing. The guidelines are based on FAO's food safety risk analysis guide, various reports from the FAO/OIE/WHO Expert Workshop on non-human antimicrobial usage and AMR, existing Codex microbiological risk assessment/management guidelines, and the OIE Terrestrial Animal Code. The guidelines were developed to be balanced and appropriate for all economies; general enough to cover all aspects of the scope, yet prescriptive enough to make a useable tool. The guidelines are available on the CODEX website under CAC/GL 77-2011.

Dr. John Stelling, Professor at Harvard University, presented a discussion of the complementary role of multi-level integrated surveillance to characterize and track evolving microbial populations to support clinical-decision making, outbreak detection, response preparedness, advocacy, public health policy, research, and capacity-building. The presentation also included a brief history of WHONET software and collaborations.

Routine clinical laboratories generate a richly detailed window into evolving microbial populations in real time. Yet this resource remains largely untapped and underutilized. The use of a common software supports local, domestic, regional, and global collaboration and analyses to support: recognition, tracking, and containment of emerging threats; cost effective care; public health policy, interventions, and advocacy. Microbiology Data Management could Enhance the use of local data for antimicrobial policy, infection control and for laboratory quality assurance. We should promote collaborations for domestic and international networks. A core element to WHONET's success has been BacLink's ability to capture and standardize data from existing IT systems. Surveillance is the key needed to:

- Track changing populations of microbial pathogens by the identification of new strains, outbreaks; trends in resistance and infection and by understanding emergence and spread of microbial subpopulations.
- Quantify the toll of resistance on human health
- Inform therapy recommendations.
- Document risk factors for emergence and spread of resistance, including animal husbandry and food production practices.
- Guide policy and resistance containment interventions.
- Evaluate the success of public health interventions.
- Energize political commitment and resources to containment efforts.
- Assess and guide continuous quality improvement and stewardship in diagnostic services.

Phenotypes are valuable strain markers, which improve detection of new threats and outbreaks. Results are available and already paid for so they should be utilized! Phenotype "fingerprinting" improves the specificity, sensitivity, and timeliness of outbreak detection algorithms. WHONET and Next Generation Sequencing Technologies build collaborations between clinical laboratories and sequencing centers. Use WHONET to flag important isolates, save the isolate for sequencing, integrate priority gene/genomics results into WHONET and observe resistance and virulence genes and predicted resistance phenotypes.

WHONET web-based platform is a centralized software configuration, optimization, data storage, and processing by trained IT and epidemiological staff, which are not always available at local levels. It provides real-time domestic and international data management with automated analysis and feedback on local and regional trends/outbreaks/ new threats. With potentially global data accessibility depending on desired configurable levels of system access to appropriate data (isolate-level patient details; de-identified data, aggregate trends, etc.). It gives opportunities for cloud-storage and "Big Data" management.

Dr. Jaap Wagenaar, Professor at Utrecht University, gave a presentation on the coordinated interventions designed to improve and measure the appropriate use of antimicrobials in veterinary medicine.

Antimicrobial stewardship has many characteristics, but there are 3 main ones

- Correct indication for treatment. In the Netherlands we are working with a lot of guidelines so that you can know when you have to treat the animals with antimicrobials. In the medical sector, people are far head from the veterinarians are and much more familiar with this issue.
- Good outcome, no excess mortality. Prudent use is not always no use.
- It's also important to have minimum side effects, including effects antimicrobials could have of the kidneys or other fiscal illness, but resistance is also included in the side effects.

In the Netherlands we are not allowed to use antimicrobials in animals for prophylaxis, when there is no disease. When we have few animals that have a disease in a flock, then you can start using antibiotics, all though this is always under discussion, is this prevention or is it treatment? If we are talking about prudent use, the use of antimicrobials as growth promotors is forbidden in the EU.

In the Netherlands we are applying the precautionary principle, we can't wait until we find out all of the details about resistance until we do something, we have to do something now. As veterinarians we have the responsibility to go as low as possible with the use of antimicrobials in animals. In the Netherlands, in 1994 we started to notice the effect the use of antimicrobials in animals could have in antimicrobial resistance in humans, because of a publication showing the resistance of campylobacter to fluoroquinolones. Not that much happened for a couple of years. In 2006, in the whole of the EU, the growth promotors were not any longer allowed. In 2009, there were two publications showing the ranking of the Netherlands with other economies regarding the use of antimicrobials in animals (highest of 10 European economies) and in humans (lowest of the European economies). This was a big trigger to start changes in the animal sectors. In 2011 there was a mandatory 20% reduction in antimicrobial use, 50% for 2013 and 70% for 2015. All antimicrobial use in farms should be transparent from 2011 onwards. We have to have a 1:1 relationship between farmers and veterinarians, this means that if a farmer request for antimicrobials and a veterinarian is not willing to provide these, the farmer cannot get these from another veterinarian, The Dutch Health Council, he advisory board for the Ministry of Health, published in 2011 recommendations on anitimicrobial use in animals. Most of the recommendations were implemented laws e.g. regarding the use of the critically important list of antimicrobials for human use, based on the WHO list. We have a definition of first, second and third choice antimicrobials, based on the selection of antimicrobial classes for ESBLs. The Dutch Domestic Reference Laboratory for Antimicrobial resistance reports annual trends of resistance in commensal E. coli. As all prescription data are available at farm level there can be a bench marking of usage for both farms and veterinarians. Veterinarians can look on the web and see how much they use with respect to their colleagues. We can see a huge reduction on the sales of antimicrobials thanks to all these measures followed by a reduction in antimicrobial resistance in commensal E. coli in the animal production sectors 3rd and 4th generation cephalosporines and fluoroquinolones are almost not used any longer in production animals.

Dr. Peter Smith, Professor at University of Ireland, gave a presentation on antibiotic therapy is an essential component of the farming of aquatic animals and resistance to antibiotics is the major factor limiting the success of such therapy. Data on the susceptibility or resistance of the bacteria isolated from aquatic animals is essential if economically sound, rational and prudent decisions are to be made in the choice of agent to use on farm. Responsible use of antibiotics also requires that the frequencies of resistance consequent of antibiotic use are regularly monitored. The use of internationally standardised testing methods and consensus derived interpretive criteria are essential if meaningful susceptibility data is to be obtained.

The major factor in driving the increase in the frequency of antimicrobial resistance is the use of antimicrobial agents by humans. Reduction in the use of antibiotics, and the elimination of imprudent and irrational use, must therefore lie at the center of any attempts to control increases in resistance. Much of the use of antimicrobials in aquaculture is not prudent or rational. This is also true of the use of antimicrobials in humans and land-based animals. The Improved prudence requires:

- Education
- Provision of advisory and technical services
- Changes in on-farm practices

Addressing these factors will have major impacts on antibiotic use and the emergence of antibiotic resistance. These factors are globally important. Their appropriate resolution will require actions specific to each local situation.

Laboratory methods for measuring in vitro susceptibility (MIC and disc diffusion) were developed over 50 years ago. They are very easy to perform. Using in-vitro susceptibility testing to detect resistance, is a two step process: Obtain a measure of in-vitro susceptibility (disc diffusion or MIC) and interpret the meaning of that value (resistant or sensitive). Susceptibility tests are not robust. The results you get are totally dependent on the protocol you use: media, temperature, inoculation, time. Accordingly, it is necessary to standardize test protocols, because we need to be able to compare susceptibility data, generated in the same laboratory at different times and by different workers; and also the data generated in different laboratories and different economies. We need internationally agreed criteria for attributing meaning to susceptibility data. For this Clinical and Laboratory Standars Institute: CLSI guidelines can be used.

On the other hand, there are different laboratories using the same test protocol, but may still generate numerically different data. For each susceptibility test protocol the acceptable range of results for reference strains are set. Everyday they test strains, but laboratories must also test reference strains. The results are valid only if the results with the reference strains are within the acceptable range.

Dr. Enrique Perez, Senior Advisor Foodborne Diseases and Zoonosis at PAHO, presented a description of the capacity building activities related to integrated surveillance of antimicrobial resistance (training courses and technical support to set up domestic programs on integrated surveillance of antimicrobial resistance) and on collection of antimicrobial usage data.

WHO's vision is for every economy to have a surveillance and response system where data on foodborne diseases from different sectors across the food chain is routinely shared and the data is routinely used to conduct continuous risk analysis to guide interventions that will ultimately reduce the burden of foodborne disease in human populations. Examples of different stages on the road to surveillance are given, economies are suggested to carry out a SWOT (Strength, weakness, opportunities and threats) analysis to asses their current position to be able to map out their goals for the future.

The manual provides economies with options for strengthening their current surveillance and response for foodborne diseases, and to integrate this within the existing domestic surveillance and response systems. It will enable economies to:

- Assess the stage of development of their surveillance and response system in relation to foodborne diseases and map out how this could be consistent with domestic needs, priorities and aspirations.
- Identify the priorities for developing their surveillance and response system.
- Make appropriate decisions about resource allocation for foodborne disease surveillance and response activities.
- Facilitate multi-sectoral collaboration between all the stakeholders involved in disease surveillance and food safety.

The manual includes all aspects of surveillance, rapid risk assessment of events, response, investigation, and multi-sectoral collaboration related to foodborne hazards (e.g. microbial, chemical and radiological) that affect human health. The primary audience for this manual is expected to be public health professionals such as surveillance and response staff, laboratory staff and food safety staff who are usually located within the Ministry of Health or human health sector.

Dr. Lisette Lapierre, Assistant Professor at the Faculty of Veterinary and Animal Sciences of the University of Chile (FAVET), presented the general results of the survey carried out to gather the information or this project. The Survey was made up of 46 questions, divided into 4 topics:

1. General information about the use of antimicrobials and the actions that are taken.
2. Integration of human health, animal health and food production.
3. Legal and regulatory aspects concerning antimicrobials and resistance surveillance systems.
4. Existence, permanence and funding of surveillance systems in humans and animals.

Some of the main results of the survey where discussed and presented in the form of graphs. In conclusion, there is a better understanding of the implications of the emergence of the AMR in the area of human medicine than in the field of veterinary, agriculture and food production. Most economies have agencies that register and authorize veterinary drugs (94%) but only 38% carry out traceability of these drugs. The 56% of the economies have a surveillance system for antimicrobial resistance in humans and/or animals. In the majority of them, these systems are developed only in bacteria isolated from humans. Of their surveillance systems, only 50% of the economies have developed concrete actions after the proper analysis have been carried out during time. Of the economies that have surveillance programs for antimicrobial resistance in animals, only 25% have developed concrete actions after the proper analysis have been carried out during time. The main issues that prevent concrete actions from being taken or surveillance programs to be set up are the lack of resources to take actions on this issue, and the lack of audit of antimicrobial use in farms and veterinary practice.

Session 2: **Where are we?**

The objective of this session was to strengthen technical competence of APEC economies´ representatives working in the areas related with AMR. This objective will be addressed by the lectures given by the invited experts that will participate in the workshop; these experts will provide APEC economies´ representatives with the tools to address this public health problem in order to work towards harmonized and standardized methodologies. Increase understanding of the control strategies of emergence and spread of AMR that have been used by other economies in the region and international organizations in order to improve economies' control measures and regulatory oversight of this hazard.

Participants included APEC Members from Indonesia, Thailand, Chile, The United States, Canada and Australia. It also featured the presentations from delegates from FDA, Colombia, The Netherlands and Ireland.

Dr. Imron Suandy, Head of Section for Animal Product Testing, Ministry of Agriculture, Indonesia, presented a brief description of the antimicrobial resistance situation in Indonesia. Indonesia has a population of 241 million people; it has more than 17.000 islands, 1.900000 km2 of land, 7.900.000 km2 of ocean and $3,500 GDP/capita. Located between 6 north latitude until 11 south latitude, and from 9 until 141 east altitude; Divided by the equator line. Indonesia territory is laid across 3,977 miles between Indian Ocean and Pacific Ocean and between two continents Asia and Australia.

The population of different species of livestock was discussed, broiler chicken have the largest population with 1.355.288 chicken in 2013. In Indonesia 6,47 kg of meat, 9,53 kg of milk and 5,61 kg of eggs are consumed are consumed per capita each year. With regard to the use of veterinary drugs in the economy, 45,7% are used as additives in animal feed, 31,45% are used in biological agents and the remaining 22.85% are used with pharmaceutical purposes. In 2011 they conducted a program to monitor AMR in West Java, in 2012 the program was extended to al Java islands. In 2015.1016 they are developing a Guideline of Domestic Monitoring-Surveillance Program in animal health sector, extend to monitor AMR in live animals, gathering information, conducting communication and collaboration, developing capacity building in 8 regional veterinary laboratory).

Politically, AMR is not priority so it's difficult to convince decision makers for financial issues. There is easy access to purchase drugs without prescription. There is no integrated surveillance system to control antimicrobial use and AMR. Most farmers (30%) do not have access to veterinary assistance. The One Health approach is difficult to apply and needs a transition.

Dr. Mintra Lukkana, Veterinary Officer at the Ministry of Agriculture and Cooperatives (MAOC), Thailand, presented a brief description of the antimicrobial resistance situation in livestock in Thailand. Department of Livestock Development (DLD), MAOC, a Domestic Veterinary Authority of Thailand, is responsible for all activities on control and prevention of AMR in Thai livestock:

- Prevent infection of livestock animals
  - Disease control program
  - Compartment system
  - Biosecurity measures for farms
  - Promote vaccination
  - Promote farm standard: With private veterinarians trained and licensed by DLD, health management programs of animals under the supervision of veterinarians. Animal treatment must comply with the "Code of practice for control of the use of veterinary drugs, Ministry of Agriculture NO.9032 in 2009" compliance with Codex CAC/REP38-1993. Animal movement permit by checking the documents and records.

- Monitoring plan
  - Coordinate the monitoring activities of the central, regional, provincial and district livestock offices.
  - Sampling from farms, slaughterhouses, meat and meat products.
  - Traceability system of livestock products.
  - Drug residues: including limitation of types and levels of veterinary drug residues (MRLs adopted from codex) and prohibited substances
  - Post marketing control of veterinary antimicrobial drugs: cooperation with THAI-FDA and sampling veterinary drugs at pharmacy stores for quality testing (340 samples/year)

- Surveillance data on AMR & AMU
  - AMR containment multidisciplinary committee and AMR surveillance working group: develop Domestic Veterinary AMR Surveillance Program, reduce antimicrobial drug usage, harmonize and implement standard method for AMR testing in livestock
  - Vancomycin-resistant enterococci experience: Thai Government banned the use and import of avoparcin mixed feed on 15 July 1998, DLD has established measures for VRE control and surveillance for the whole poultry meat production chain. Prevalence of VRE in Thai poultry industry is currently very low. Continuation of VRE surveillance in both domestic and export markets

- Project of surveillance of Salmonella spp. in meat and meat products from slaughterhouse, meat processing plants and markets.
- Technical cooperation with Food and Agriculture Organization (FAO) of the United Nations
- Surveillance Resistance bacteria and resistance genes in food chain
- Surveillance data on AMU (under development)

Dr. Juan Carlos Hormazabal, Head of Infectious Diseases Sub-department at the Public Health Institute, Chile, gave a brief description of the antimicrobial resistance situation in Chile.

The indiscriminate use of antibiotics increases the bacterial resistance and forces the use of more expensive alternatives.

The Chilean Ministry of Health is regulating the consumption of antibiotics since September 1999. Restricted sale of antibiotics by law: only prescribed by a doctor. The regulatory framework in Chile defines the objectives, epidemiology and as a laboratory network is structured to build monitoring laboratories in the economy, two major components exist:

- Laboratory-based system
- Environmental monitoring component

The main challenges on a domestic level are: to have a system of integrated information and surveillance. For this there are New Guidelines for Health Care Associated Antimicrobial resistance, this system is based on clinical and epidemiological surveillance and laboratory based surveillance. Other main challenges are the technical challenges, this consists on strengthening the capacity to rapidly detect, and accurately identify potentially epidemic antimicrobial resistance mechanisms. In the future we want to achieve an integrated look, considering the following points: Lack of Formal antimicrobial resistance surveillance system in enteric pathogens from the agri-food industry, with sporadic Initiatives:

- Agriculture-Food Industry Associations
- Research Institutions, Universities

The molecular tools used in surveillance and diagnosis can become mobile systems for emergency PCR for enteric outbreaks, as in the case of an earthquake in our economy. Besides the importance of robotization to decrease the response time. It should have a formal integrated any cross look on antimicrobial resistance food. We must seek exhaustively and conduct research. You need to combine strains and do all in the same laboratory, that's integrated surveillance.

Dr. Patrick McDermott, Director of the National Antimicrobial Resistance Monitoring System at the FDA, presented a description of the U.S. NARMS program and its role in evaluating resistant foodborne bacteria. The NARMS program objectives are to monitor trends in antimicrobial resistance among foodborne bacteria from humans, retail meats, and animals; disseminate timely information on antimicrobial resistance to promote interventions that reduce resistance among foodborne bacteria; conduct research to better understand the emergence, persistence, and spread of antimicrobial resistance; assist the FDA in making decisions related to the approval of safe and effective antimicrobial drugs for animals. It includes 3 different components:

- CDC: Human isolated testing, bacteria isolated at the state laboratory and sent to CDC for susceptibility testing and additional analyses (Non-typhoidal Salmonella, Campylobacter)
- FDA: Retail meat testing, Salmonella (all meat types), Campylobacter (poultry). E. coli, Enterococcus.

USDA: Samples taken by FSIS veterinarians and inspectors at FSIS-regulated plants and establishments. Cecal samples better reflect animal status and less confounded by plant events. There is a randomized, domesticly representative testing of slaughterhouses. They have the ability to distinguish production classes.

For the drug selection they choose drugs that are important in veterinary medicine, important in human medicine, important in both veterinary and human medicine, drugs that are epidemiologic markers (such as chloramphenicol) or with harmonization with CIPARS. With this information they conduct research and assist the FDA, some examples of cases in which the information was used to take different measures were discussed.

Dr. Rebecca Irwin, Director of the Canadian Integrated Program for Antimicrobial Resistance Surveillance Division of the Public Health Agency of Canada, presented a description of the Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS). Formally established in 2002 CIPARS monitors resistance and antimicrobial use along the food chain. In the early stages of program development the link between animal and human AMR was controversial and was not considered a food safety issue. There was no existing infrastructure for AMU or AMR surveillance along food chain in Canada. This required a new approach and design. CIPARS objectives are to provide unified approach to monitor trends in antimicrobial resistance and antimicrobial use in humans & animals; disseminate timely results; facilitate assessment of the public health impact of antimicrobials used in humans & agriculture; and allow accurate comparisons with other economies that use similar surveillance systems. CIPARS is a voluntary program with participation from human and animal health stakeholders, the agri-food industry, academia, and provincial and federal governments. The full implementation of CIPARS took many years to accomplish with component parts being added as partnerships were established and as funding was made available. For example, human antimicrobial use information started in 2003, but animal antimicrobial use information started in 2004 with domestic distribution data, and in 2007 for antimicrobial use data at the farm level for swine. Antimicrobial resistance data was available in 2002 for abattoir chicken, beef, and swine, but retail AMR data was added incrementally across selected provinces in subsequent years.

The farm component of CIPARS is a more recent addition to the program and provides the most important source of valid antimicrobial use information. This works as voluntary participation by producers enrolled by contracted veterinarians (confidentiality and biosecurity concerns addressed). Farm samples are collected for AMR testing and animal health and farm management data is collected through the application of questionnaires. Antimicrobial use information is also provided to CIPARS on an annual basis from the Canadian Animal Health Institute which represents pharmaceutical manufacturers of animal products in Canada. From this data, CIPARS was able to report that in 2013, 79% of the medically important antimicrobials distributed for sale were for use in animals; this quantity produced for animals represented 3.8 times the quantity for people. Given that there are about 18 times more animals than people, when adjusting for populations and weights this translates into about 1.4 times more antimicrobials distributed/ sold for animals than for people..

The 13 years of CIPARS experience has told us that creation of a domestic integrated surveillance system is possible and can support several objectives; it helps preserve effectiveness of antimicrobials for human and animal health; it provides data to support source attribution and intervention studies; it provides relevant Canadian data to support pathogen reduction strategies and means to monitor the prevalence of primary foodborne pathogens over time; it supports antimicrobial stewardship programs; and also supports international efforts to build integrated AMR surveillance programs. In animal health it helps with the pre-approval and post-approval monitoring of antimicrobial agents for veterinary use and in the international trade arena, surveillance is considered integral to CODEX risk analysis framework for AMR.

Dr. Betty San Martin, Professor at the Faculty of Veterinary and Animal Sciences of the University of Chile (FAVET), presented a brief description of the antimicrobial situation of antimicrobial use in Chile. Bacterial resistance is a problem of limitations on treatment options (multidrug-resistant bacteria). As long as no other therapeutic alternatives are available, antimicrobials remain the main therapeutic tool. Bacteria acquired resistance mechanisms simultaneously to different groups of antimicrobials. Resistance genes are transferred between bacteria from different species and genus through mobile genetic elements. Intestinal macrobiotic is an ecosystem reservoirs of resistance genes, therefore it's necessary to establish an action plan. The action plan to contain bacterial resistance consists on:

- Promoting good practices in antimicrobial use under veterinary supervision
- Promoting the development of monitoring programs
- Encouraging research for the development of new therapeutic tools.

Regarding actions implemented at the domestic level to control bacterial resistance, the domestic agriculture and livestock service (SAG), regulates the administration of veterinary drugs in Veterinary Drug Registration: Modified by Supreme Decret N° 25 of 2005. The domestic fisheries service (SERNAPESCA) regulates use veterinary drugs by the regulation of protective measurements for the eradication and control of high risk diseases in aquatic species, D.S. N° 319/2001. It also includes the use of pharmaceutical products regulated in fish and aquaculture, and performed an antimicrobials reduction plan through its proper use, reducing piscirickettsia in the south of Chile.

Dr. Pilar Donado, Leader of Food Safety and Quality Unit at Colombian Corporation of Agricultural Investigation, Colombia, presented a description of the Colombian Integrated Program for Antimicrobial Resistance Surveillance (COIPARS) that was a established as a pilot project to monitor AMR on poultry farms, slaughter houses and retail markets.

Colombia, as an emerging economy, has a high pressure of infectious diseases with a high poverty rate. There is a rapid urbanization and in some cases poor hygiene measures. There is a high demands of animal protein that is being cover by the animal industry and in many cases the volume of production is come important that food safety. Colombian regulations are not in its optimal state; in some cases there is indiscriminate use of antimicrobials. The sale of antimicrobials for human use requires prescription, but in the case of drugs for animal use, the regulation for this is made but it is still not compulsory. There is also contraband smuggling, adulteration and falsification of antimicrobials.

In Colombia in 2007 there was a fragmentation in the determination of antimicrobial resistance, the human, animal and food information was separated but we had a will to work together. We didn't have base lines in the fields of animals and food. The first step to start this project was the engagement of all the stakeholders to plan the project. We formed a scientific committee to decide how we would work. The support of the WHO/PAHO was fundamental for this step because they were the ones who contacted us with the directors of the successful AMR programs as CIPARS, DANMAP and NARMS. We did a strategic mapping of the food chain and decided to work with the chicken industry because it was the most standardized animal industry in the economy, and it had a high risk of antimicrobial use. After mapping the poultry chain we concentrated on the poultry production and retail stores. We also included all of the official institutions and universities that have to do with the use of antimicrobials. At the beginning the Colombian USDA (called ICA) gave to COIPARS the most support in terms of funds and infrastructure. CORPOICA is an academic institution of agricultural investigation. We formed a consortium including both these institutions together with the Colombian FDA (INVIMA) and the Domestic Health Institute. We also worked with Universities that had experience in AMR. From the private sector we had the input from the National Federation of Poultry Producers and from the largest supermarket chain in the economy.

We started our program in the different steps of the poultry production chain: farms, slaughter houses and retail stores. We first started with only 3 bacteria, Salmonella as the pathogen and E.coli and Enterococcus as indicators. With this program we validated sampling methods. In 2008 we started sampling only 2 departments on Colombia and in 2013 we were already sampling from 18 departments. This system has now been established as a strategic plan in the Colombian Agricultural Institute and we are looking at a regulation change for growth promotors in the poultry industry. Our results are published in different international journals and with them we could increase of awareness on the AMR issue in the region, in the production sector, public health authorities and lawmakers and are the base for a more rigorous risk analyses. Also through the development of this project we build capacity, setting -up international standard methods in Colombia, laboratories and personal training and the development of international collaboration. Also, as said before, we are collaborating with the reinforcement of the legal framework on antibiotic usage.

Mr. Ricardo Castellanos, PhD Student at Utrecht University, The Netherlands, gave a presentation on the Different molecular mechanisms that can be responsible for the development of antimicrobial resistance. Harmonized tools for genetic analyses can help to understand the mechanisms of acquired resistance and its transfer amongst bacterial species and production sectors, and its geographical spread.

Cefotaxime is a β -lactam drug, a third generation Cephalosporin and has broad-spectrum activity, this means it's active against gram-negative and gram-positive bacteria. The enzymatic resistance to this drug is mediated by Extended Spectrum β -lactamases (ESBLs) and AmpC β -lactamases. ESBLs can be inhibited by clavulanic acid, but AmpC can't. At the molecular level of the epidemiology of β -lactamases, we have genes that give resistance to these drugs; we have ESBL genes and AmpC genes. We also have mobile genetic elements that carry genes, like plasmids, transposons and insertion sequences. Finally we also have host bacterial cells that carry genes that can be localized in the chromosomes (clonal spread) and in plasmids (horizontal transfer).

In order to assess the dynamics of ESBL and AmpC producing E. coli in the Colombian poultry chain we started using the COIPARS platform to study the molecular epidemiology Dynamics of ESBL and AmpC producing E. coli. We used Escherichia coli because it is a very good indicator of AMR in Enterobacteriaceae including Salmonella. The aim of our study was to provide the molecular characterization of genes, plasmids and strains carrying this resistance. We used the samples from the base line studies of COIPARS, they came from farms, slaughterhouses and retail. At the farm level we collected fecal samples, at slaughterhouses we collected cecal content and carcass rinse and at retail we collected meat and carcass samples. In total we collected 141 isolates from farms, 182 from slaughterhouses and 430 from retail.

We first characterized the strains at the phenotypic level, this means that we have an E.coli that is resistant to a particular drug, but we still don't know what gene is responsible for the resistance. Then we can characterize the genes in this strain but we don't know yet if the genes are located on plasmids or in the chromosome. Then we perform the characterization of the plasmid, with this we know that the resistance gene is located on the plasmid that now we know is in our bacteria. Finally we characterize the resistant E. coli level at strain level, for this we need genetic information that is in the chromosome of the bacteria.

For the phenotypic resistance we use β -lactam antibiotics provided by the Phoenix automated system, with this we can see that the bacteria is resistance, but we can't know which gene is mediating this resistance or anything else. For gene characterization we use PCR to detect the genes and then we perform sequencing of this products, this resulted in the characterization of the resistance genes. For the plasmid characterization we first confirm that the resistance genes were located on plasmids and we then characterize the plasmids based on the incompatibility group. We first have to isolate de plasmids and transfer them to an E. coli that is susceptible to cephalosporins and then we can confirm that this newly transformed E. coli was carrying the resistance gene using PCR. Finally we use PCR Based Replicon Typing (PBRT) to know that our gene is on a plasmid and in our bacteria. To perform the strain characterization we use sequence-based typing, we this we can know our gene, our plasmid an also the information of our strain.

To take integrated surveillance to a more in-depth level, we have to consider the molecular epidemiology of the resistance genes, and not only focus on the phenotypic data.

Dr. John Stelling, Professor at Harvard University, presented a summary of domestic, regional, and global AMR surveillance and EQA programs. All institutions with a microbiology laboratory and all economies should have a system for the confirming and communicating isolate results of high public health importance. All economies should routinely monitor results generated in the course of routine work, except in the lowest resource economies, these data are an excellent base for a broad-based, sustainable surveillance:

- All isolates, all sample types
- Identification of important strains, outbreak detection, trends in infection, trends in resistance
- Comprehensive data collection, selective data analysis -permits retrospective and ad hoc queries
- Improvements in laboratory capacity: quality assurance standards, education, capacity-building
- With regards to therapy recommendations, the data can be very biased

There should be targeted surveillance protocols and surveys. With many variations depending on public health/scientific needs and resources such as patient demographic and clinical details, burden of disease, specimen collection and laboratory processing. Sustainability is a significant concern, and only a few issues can be studied. In the lowest resource economies and to support outpatient treatment guidelines may be the only way to get reliable data. When there is also a routine surveillance program in place, it can be used to cross-validate, complement, and enhance findings from routine.

The AMR activities in the region of the Americas has been developing since the 1980s, when a few economies initiated subdomestic surveillance with WHONET (Argentina, Chile, Colombia, Venezuela) In the 1990s regional AMR activities for enteric pathogens were initiated and ResistNet was initiated, supported in part by funding from Pfizer. Following the withdrawal of Pfizer's trovafloxacin from the market, the economies of ResistNet launched ReLAVRA In the 2000s regional EQA coordinated by PAHO and the Malbrán Institute in Buenos Aires and there was active participation in PulseNet International. Finally in the 2010s there were new activities to integrate Next Generation Sequencing.

In the European Region, in 1997 the a WHO workshop titled " The Current Status of Antimicrobial Resistance Surveillance in Europe" was held in Collaboration with the Italian Associazione Culturale Microbiologia Medica in Verona, Italy. From the year 2000 to 2010 EARSS was coordinated by RIVM, Netherlands. From the yearr2000 to the present EQA is provided by UK NEQAS. From 2011present EARS-Net is coordinated by ECDC, Sweden. There is a European Antibiotic Awareness Day.

With regard to the AMR activities in the Eastern Mediterranean Region, since 1994 EMRO Guidelines for Antimicrobial Resistance Surveillance exist. From the year 2000 to 2005 there was a antimicrobial Resistance in the Mediterranean, a European Union-funded project using EARSS protocols. In the 2000s the REQAS Regional Microbiology EQA Scheme for coordinated by WHO-Lyon and the Central Health Laboratories, Muscan, Oman. In 2004 the WHO Workshop on Strategies for Containment of Antimicrobial Resistance in the Eastern Mediterranean Region took place in Cairo, Egypt. In 2013 a consultative meeting on antimicrobial resistance for economies in the Eastern Mediterranean Region: from policies to action, took place in Egypt.

In the African Region the primary focus has been on domestic reference laboratory capacity for outbreak-prone public health threats. EQA is coordinated by WHO-Lyon and the National Institute of Communicable Diseases in South Africa. WHO developed EpiInfo laboratory reporting application called BacteriologyLab.

In the Southeast Asia Region the primary focus has been on local and domestic capacity for routine clinical diagnostics. A regional EQA program is now being established to be run by the WHO collaborating center for antimicrobial resistance surveillance and training at the Ministry of Public Health National Institute of Health in Thailand. Assistance is provided to establish domestic AMR surveillance Integrated surveillance may address distinct sectors such as antimicrobial use and resistance in humans, animals/aquaculture, food, environment and at an industrial level. Integrated surveillance is needed to alert public health authorities of emerging threats to human health, emerging in animal populations, provide evidence for risk assessment and risk management of policies and practices in animal husbandry, food production, and food processing, evaluate the success of interventions on practices and microbial populations, build advocacy efforts and political commitment for resistance containment, guide therapy decisions in animal populations to safeguard animal health and food safety. Some examples of integrated surveillance are: DANMAP, NORM/NORM-Vet, CIPARS, NARMS, COIPARS, SVARM, MARAN, etc

Dr. Jaap Wagenaar, Professor at Utrecht University, gave a presentation on the details of the Ecology from Farm to Fork Of microbial drug Resistance and Transmission (EFFORT) project.

For surveillance systems we can consider pathogens, but we can also use commensal bacteria, or both. If we only look for pathogens, if we have a low prevalence, we will have to analyze many samples to get the strains. You can also look for E. coli because almost all the samples have E. col and it is a very good indicator. If you have your system up and running and you are looking at the pathogens and you have a good surveillance system for this, of course that you can only look at pathogens, but if you want to implement a system to see what is around I would recommend to look at the commensals because they are everywhere. Depending on you method of isolation, you can have significant difference in prevalence; you should always use methods that you can compare with others. Over the years in different economies there have been interventions made with the results of different studies with a measured effect on resistance.

Ecology from Farm to Fork Of microbial drug Resistance and Transmission (EFFORT) is an EU subsidized project. In the EU we noticed a difference in usage of antimicrobials and therefore we know that some economies are doing very well at implementing interventions in primary production. Our project questions are:

- How are AMU and AMR related to farm management?
- How are economics and animal welfare related to AMU and AMR?
- What is the relative attribution of food of animal origin to AMR exposure of humans and what effect will interventions have?
- How powerful are molecular detection techniques for AMR surveillance (in comparison to the existing system)?
- Will the development and use of a tool for AMU-intervention in primary production be feasible and effective across Europe?
- Why are some bacterial clones so successful and can we recognize them in an early stage?

The project started almost 2 years ago, we are working with 10 economies and 20 institutions including WHO, OIE and EFSA as external board member. Patrick McDermott and Morgan Scott are also on our board to critically look over our progress. Our objectives are the understanding the epidemiology of AMR in the food chain, understanding the ecology of AMR in the microbial communities, understanding the relative contribution of the exposure routes of AMR from animals to humans and understanding the economic impact and animal welfare aspects of AMR in the food chain. EFFORT will provide the animal production sector and policy makers evidence based information on antimicrobial resistance to support a sustainable animal production with minimal risks for public health.

Dr. Peter Smith, Professor at University of Ireland, gave a presentation on the use of antibiotics in the farming of aquatic animals has the potential to impact negatively on human health. Perceptions of the size of this risk will influence both the regulatory environment of global aquaculture and the acceptability of the product to the consumer and will, therefore, exert a significant effect on the economics of aquatic farming. Formal Risk Assessment is the process that attempts to provide the data that will allow the estimation of the size of the risk to move from a belief-based conjecture towards an evidence-based quantitation. A theoretical analysis will be presented that will aid in identifying the data that should be collected to facilitate a Formal Risk Assessment.

Consider two exposure pathways to bacterial resistance, the movement of resistant bacteria and movement of transferable resistance determinants, genetic elements that can move between bacterial species and potentially decrease the antibiotic susceptibility of bacteria that acquire them. In the first case it is necessary to consider the following:

- Presence of bacteria capable of infecting humans in the aquaculture environment (zoonotic aquatic species or terrestrial contamination)
- Selection of resistant variants of these bacteria as a result of antimicrobial use in aquaculture
- Transfer of these resistant bacteria to the human environment (via aquaculture products or water)
- Infection of humans
- Adverse effects resulting from the failure of any necessary antimicrobial agent therapy

The presence of bacteria capable of infecting humans in the aquaculture environment is dependent of the relatively few zoonotic aquatic species as vibrio parahaemolyticus and motile aeromonads. The Terrestrial contamination is the bigger problem in fresh water. The quantitative assessments associated with movement of resistant bacteria, may be possible with respect to specific bacterial species emerging as a result of the use of a specific drugs in specific aquatic animals in specific locations. The qualitative assessment is definitely much lower than those associated with antibiotic use in land-based animals. In addition, you should consider the movement of resistance determinants. Resistance determinants have travelled through the global microorganisms since before man started to use antibiotics. The totality of resistance determinants in an environment has been named the environmental resistance. The magnitude of the resistance has been greatly increased by the selective pressure resulting from our use of antimicrobial agents. The environmental resisted is the ultimate source of the resistant determinants in those bacteria that infect humans.

The data that we collect to perform an entry assessment are data on the concentrations and spatial/temporal footprint in the vicinity of aquaculture units of:

- Phenotypically resistant bacteria: most studied but of little relevance to risk assessment.
- Antibiotics: Detectable concentrations have been detected in the local environment of aquatic farms.
- Resistance determinants: Elevated frequencies have been found in aquatic farm environments.

This environmental resistance, its mobilization, and the conditions that facilitate its entry into human pathogens are at the heart of the current public health crisis in antibiotic resistance. Understanding the origins, evolution, and mechanisms of transfer of resistance elements is vital to our ability to adequately address this public health issue.

Dr. Patrick McDermott, Director of the National Antimicrobial Resistance Monitoring System at the FDA, gave a brief introduction into the power of whole genome sequencing to characterize resistant bacteria tracked in surveillance. Integrated antimicrobial resistance surveillance today means to isolate pure cultures from samples obtained from animals, foods & people, ship them to central laboratories to conduct a small number of expensive and labour intensive assays in batch using specialized reagents, present aggregated phenotype data over time in an integrated fashion and perform research projects to more fully characterize and compare strains, and publish the results months or years later.

Next generation whole genome sequencing (WGS) technologies have made it affordable to routinely determine the complete DNA sequence of a bacterial isolate (ca. $40/isolate). Within 2-3 years, >100,000 Salmonella WGS will be deposited annually at NCBI. Genome sequences provide a common language for analysis of all organisms. Analysing WGS data takes more time than generating data. Because any phenotype can be decoded from the genome, WGS is replacing many traditional diagnostic and subtyping laboratory methods that require dedicated reagents and specialized training. Serotyping, PCR, strain typing, virulence profiling, and antibiotic resistance patterns can all be realized in a single analytical workflow. WGS provides the highest practical resolution for comparing microbial strains. This makes it possible to identify links between clinical illness and specific food and environmental sources of contamination that were previously missed and identify sources of contamination more quickly, to resolve outbreaks with fewer clinical cases, and to improve attribution of sporadic illnesses. WGS will make obsolete the different surveillance systems based on different methods (PulseNet, NARMS, domestic pathogen reporting). A common data reserve will be mined for different purposes. The development of international open source databases will empower.

WGS for sentinel surveillance work on a global scale. Introduction of culture-independent diagnostic is driving metagenomic approaches to sample testing, diagnosis and surveillance.

There is a strong correlation between resistance phenotypes and genotypes for nearly all antimicrobial agents. Comprehensive resistance genotypes of all tested bacterial strains were identified and the resistance mechanism for each antimicrobials tested was defined including some of intermediate susceptibility.

Reasons for disconnect

- Breakpoints are imprecise
- Experimental and analytical error
- Variable gene expression level
- Unknown mechanisms

WGS Surveillance has many strengths, it can serve as the single assay of surveillance (such as NARMS) and supplant multiple methods, saving time and money, it also provides genome/allele/nucleotide surveillance. WGS weaknesses are that it can only identify known resistance genes/ mutations, novel genes or variants may not be detected if low homology to known ones, it needs a comprehensive, accurate, highly curated and updated resistance gene database, it requires significant investment in IT infrastructure, expertise are needed to analyze data and fragmented genomes complicates identification of resistance elements.

Mr. Steve Crossley, Manager – Scientific Strategy, International and Surveillance Section at Food Standards Australia New Zealand (FSANZ), presented Australia's 1st National Antimicrobial Resistance Strategy focusing on proposals for Integrated AMR surveillance and the importance of food safety. FSANZ is a bi-domestic expertise-based government agency that develops food standards.

In a 2014 poll of Australian workers, 65% believed that taking antibiotics would help with recovery from cold or flu. One in five people expect antibiotics for viral infections like a cold or flu. Nearly 60% of General Practitioners (GPs) prescribe antibiotics to meet patient demands or expectations. In contrast to the relatively high use of antibiotics in human medicine, Australia has a comparatively low antibiotic usage in food producing animals. From 2005 -2010, average usage in Australia was 15mg/PCU (population corrected sales usage) per year for food animals. In 2012, the median usage in EU and EEA economies was 62mg/PCU (range 4 -397 mg/PCU)- Pre-market registration (APVMA) and strict controls on all vet drugs. 97% of veterinary sales were for food producing animals, of these 5% for growth promotion, 45% for therapy and prophylaxis and 51% for control of coccidiosis in chickens.

Australia's food safety system has strict requirements to manage bacterial levels (both resistant and non-resistant) along the food production and processing chain, regulatory controls at all levels of government and industry standards and guidelines. Australia has also had a strong pre-market registration system for vet drugs for mny years.

The objectives of Australia's 1st National AMR strategy for 2015 -2019 relate to the following seven areas:

- Increase Awareness
- Antimicrobial Stewardship
- One Health Surveillance
- Infection Prevention & Control
- National Research Agenda
- International Partnerships
- Governance

An implementation plan for the new Strategy is under development (2016). An on-going domestic surveillance system will be a key component..

Dr. Morgan Scott, Professor at Texas A&M University, gave a presentation on the existing and potential research agendas, in both biological and social sciences, as well as policy aspects that impact the highly complex problem of antimicrobial resistance.

We seek practical and affordable 'solutions' that agricultural and food producers can readily adopt, preferably, within the context of existing or easily adaptable management systems. There have ben many U.S. regulatory actions, in the late 1990s the FDA banned the extra-label uses of fluoroquinolones and glycopeptides and in 2012 the same occurred with cephalosporins. There has been a historical succession of mandates and recommendations culminating in the period from 2005 to 2011 with the lists from WHO and OIE which have on-going updates and revisions with WHO and OIE (and FDA).

The WHO Critical List acts as risk management options and risk communication and prioritizations among other uses. Plus, when a new class of [human] drug comes on the market, it should be considered critically important from the outset unless strong evidence suggests otherwise. Existing drugs such as carbapenems, linezolid, and daptomycin, which are not currently used in food production, should likewise not be used in the future in animals, plants, or in aquaculture.

Antibiotics enhance the health and well-being of humans and animals, there is overuse/misuse of antibiotics in both human and animal settings, protecting the efficacy of antibiotics for future generations is a good thing to do. Some say that Human medicine takes precedence over veterinary medicine and animal agriculture, that precautionary principle should prevail, increasing order of defensible use: growth promotion, prophylaxis, control, treatment and that drugs deemed critically important to human medicine should not be used at all in animal agriculture. Another point of view is that antibiotic treatment should be viewed as a last resort, that prevention and control of disease in food animals improves both animal and human health and that antibiotics help improve food security in a world with growing needs.

Session 3: **How to implement a program?**

The objective of this session was to build competency and capacity in AMR surveillance through knowledge transfer between APEC economies with ongoing surveillance programs and other developing APEC economies that do not have an ongoing surveillance program on this subject.

Participants included APEC Members from: Australia, Canada, Chile, People´s Republic of China, Indonesia, Malaysia, Mexico, New Zealand, Papua New Guinea, Peru, The Philippines, Thailand, The United States, Viet Nam.

Dr. John Stelling, Professor at Harvard University, gave a tutorial on WHONET use and what a good platform system management must have. And a demonstration of WHONET's features for laboratory configuration, data entry, data analysis, and data sharing. Also the import of data from existing information systems using BacLink and recommendations about what any antimicrobial resistance data system management must have.

Group Session:

Dr. Constanza Vergara, ACHIPIA. Members were divided in three working groups, and should answer the following two questions:

1. Mention the difficulties you believe exist in your economy, to implement an integrated AMR surveillance program.
2. Which actions should be taken, in short and long term, to implement an integrated AMR surveillance program in your economy?

Long term:

Short term:

At the end of the session each group had 15 minutes to present their conclusions (via a small power point presentation).

The first group was formed by APEC Members from: Canada, USA, People's Republic of China, Mexico and Papua New Guinea.

Question 1:

- Lack of education and awareness on the effect AMR on the food

security, public health, environmental and the whole economy.
- Lack of cooperation to authorities within the economies.
- Lack of understanding, fear of participation by stakeholders.
- AMR is buried under food safety agenda
- AMR is not a priority of government
- Lack of funding
- Lack or deficiency of technical expertise and Infrastructure (Laboratories)
- Lack or deficiency on better governance of medicinal and veterinary products.

Question 2:
Short Term:

- Gathering important stakeholders to discuss and come to one action plan (PNG, China).
- Use of collaborative database like WHONET.
- Identify existing information, check who is doing what.
- Determining the antimicrobial usage (AMU) in human and veterinary fields.
- Understand the food system/chain and distribution, consumption.
- Understanding the volume and dynamics of Issues import and export commodities.

Long Term:

- Bring in representative sampling.
- More studies needed on methods to incorporate aquaculture into integrated surveillance which also include impact of AMR to the environment.
- Bringing the environmental aspect of AMR both terrestrial and aquatic farming.
- Pilot studies on the positive impact of mitigation activities e.g. Combating Counterfeit drugs.
- Reinforce existing regulations to support AMR reduction such as prudent use and responsible use of antimicrobials.

The second group was formed by APEC Members from: USA, Indonesia, Peru, The Philipines and Viet Nam.

Question 1

- Lack of awareness and link among stakeholders (i.e samples, agreements).
- Lack of political will and change of administration (commitment).
- Governance and institutional issues.

- Lack of law enforcement in AMU and interventions.
- Lack of laboratory capacity.
- Data problem (collecting, sharing, burden of illness, AMU, lack of baseline data.
- Lack of harmonized methodology.
- Lack of expertise and Limitation of fund and human resources.

Question 2:

Short Term:

- Getting agreement in One Health vision and maintain the commitment.
- Promote awareness of WHO GAP.
- Training human resources.
- Validation and unification of methods.
- Additional human power.
- Get support from human health sector.
- Build sustainable capacity.
- Standardization of methods (internationally).
- Involve the private sector to share responsibilities.
- Begin with the most standardized industry that could have the biggest impact.
- Public meetings stakeholders.
- Networking in each economy.
- Establish a feasible Pilot Project to show the situation and the importance.

Long Term:

- Show the value of other aspects beside AMR (Food safety).
- Networking (Establishment a network of laboratories and institutions).
- Inclusion new technologies (WGS).
- Assess the Impact about quality and needs – get credibility.
- Work with other economies in the region to share experiences and practices.

The third group was formed by APEC Members from: USA, Australia, Malaysia, Chile and Thailand.

Question 1:

- Raise awareness at every step of production chains and stakeholders.
- Trigger Political commitment.
- Implementation of tools to measure use and consumption of antimicrobials at the farm level.

- Improve education, in different production systems in AMR and also antimicrobials USE.
- Political commitment.
- Modernize regulatory framework, share information.
- Improve Technical part, diagnosis and interpretation of data.
- International standards, quality assurance.
- Education.

Question 2:

Short Term:

- Use available information and isolates to have an integrated baseline of AMR: be prepared for windows of opportunities (MARAN example).
- Share standards, create a network of collaboration at the laboratory level.
- Share between economies communication experiences and also promote technical communications.

Long Term:

- Can Chile take the lead on proposing a course on One Health, International organizations can provide an open virtual campus.
- Consider local needs, aquaculture for example.
- Integrated surveillance: proposed to politics for funding.
- 3rd of December the global burden of foodborne diseases will be launched, with global estimates divided by regions.
- Use the domestic focal points.
- OIE has some tools to strength One health issues.

Workshop Conclusions & Closure

Mr. Michel Leporati, Executive Secretary, Chilean Food Quality and Safety Agency-ACHIPIA

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Pre Workshop Survey Analisis

To gather the information for this workshop a survey was sent out to all of the APEC Economies. We received 17 responses including; Australia; Canada; Chile; China; the Philippines; Hong Kong, China; Indonesia; Japan; Malaysia; Mexico; New Zealand; Papua New Guinea; Peru; Chinese Taipei; Thailand; USA and Viet Nam. This represents 81 % of the call.

The Survey was made up of 46 questions, divided into 4 topics:

- General information about the use of antimicrobials and the actions that are taken.
- Legal and regulatory aspects concerning antimicrobials and resistance surveillance systems.
- Existence, permanence and funding of surveillance systems in humans and animals.
- Integration of human health, animal health and food production.

Within the first topic, it was found that the zoonotic bacteria or bacteria transmitted by food, causing a greater impact on public health in the APEC region are: Salmonella, Campylobacter, Listeria monocytogenes and E. coli. With regard to antimicrobial resistance, we asked about the awareness of the subject in the field of resistance in humans, "high awareness" was recorded in 25% of cases, "medium" by the same percentage, " low "by 38% and the rest did not know. In the case of awareness of the contribution that the use of antimicrobials in agriculture and veterinary has to resistance in bacteria that cause disease in humans, 6% answered "high awareness", 44% "medium", 44% "low" and the rest did not know. Then we asked the same question but with specific groups of people, in which the highest awareness of the issue was registered among academics, workers in the health area, the pharmaceutical industry and government institutions. While the lowest awareness according to the responses, was within the general public and the media. In the specific case of the professionals in the field of veterinary medicine, "high awareness" was recorded in 44% of the cases, "medium" in 56%, "low" in 6% and the rest did not know. Among the factors they thought were most influential to the emergence and development of antimicrobial resistance, 50% replied that economies do not have sufficient resources to take action on the issue, 44% of responded it is because of the lack of oversight of the use of antimicrobials in veterinary medicine and agriculture, and 38% responded that there are few alternatives to antibiotics, the same percentage answered that there is a lack of legislation regulating the use of antimicrobials, antimicrobials for veterinary use are sold without prescription, and that critically important antibiotics for humans are used in veterinary medicine.

Regarding the second topic, “legal and regulatory aspects concerning antimicrobials and resistance surveillance systems”, we can say that 81% of the economies have domestic standards or guides to address the issue of antimicrobial resistance, however only 56% of them have surveillance system for antimicrobial resistance and in the same percentage there are laws to address this problem. In most economies with surveillance systems, the institution in charge of these surveillance systems is the government, sometimes accompanied by the private sector, universities or others that are unspecified. In 50% of the economies there is a coordinating mechanism at a domestic level, responsible for organizing the activities related to antimicrobial resistance. 100% of the survey respondents said that there is a domestic regulatory authority responsible for the registration and authorization of medicines for use in both humans and animal use. However, only in 38% of these economies there is a program of traceability (serial control throughout the food chain) of antimicrobial use. In 63% of the economies there are rules for monitoring antimicrobial resistance in animal production environments. For 49% of the economies, the list of authorized medicines for veterinary use is their own legislation harmonized with the Codex Alimentarius, in only 30% its only their own legislation and the rest do not know. In 69% of the economies there are control programs for veterinary drug residues in food and/or environment. In only 50% of economies there is a list of essential drugs for human use. In 81% of economies, the sale of antimicrobials without a prescription is not allowed in the case of human drugs, in the case of antimicrobials for animal use, this figure drops to 44%. The mechanisms used by the Domestic Regulatory Authority in economies that control the sales of these drugs with prescription only are; in 50% of economies sale prescription and in 44% sale with retained prescription. Another question related to the issue was whether there was a program of mandatory reporting of infectious diseases in humans, where 87% said that there was a program, but only in 50% of these antimicrobial susceptibility results are included in these notices. In 62% of the responses they said there was a management plan within the monitoring program, but only by 43% this plan includes indicators an/ or goals.

Another area addressed were the issues related to the “existence, permanence and funding of surveillance systems in humans and animals”. Only in 38% of the economies there is a domestic report on the progress of resistance updated over the past 5 years. We asked if there are reports of epidemiological surveillance, updated in the last five years, on antimicrobial resistance in humans and animals. For human 69% said that there were reports and in animals it was only 44%. In 50% of economies concrete actions are taken with the results of these reports in the area of human medicine, in the case of the veterinary area this figure is 25%. In 56% of economies they have conducted educational campaigns for the appropriate use of antimicrobials in humans, and 50% have been conducted in regard to the use in animals. In 87% of the economies there is an official domestic reference laboratory that performs or could perform antibiotic sensitivity tests, 81% participate in a program of external quality assessment for antimicrobial susceptibility testing (interlaboratory tests). In most APEC economies, financing activities related to antimicrobial resistance are public. In the case of research on this topic, financing is shared between the government (69%) and universities (63%), the latter being mostly public.

The last area addressed by the survey was the "integration of human health, animal health and food production", it was found that in general, most economies have the tools to conduct surveillance of antimicrobial resistance only the area of human medicine, and only in more advanced economies these measures extend to the area of veterinary medicine and agriculture.

From this survey we gather that there is a better understanding of the implications of the emergence of the AMR in the area of human medicine than in the field of veterinary, agriculture and food production. Most economies have agencies that register and authorize veterinary drugs (94%) but only 38% carry out traceability of these drugs. The 56% of the economies have a surveillance system for antimicrobial resistance in humans and/or animals. In the majority of them, these systems are developed only in bacteria isolated from humans. Of their surveillance systems, only 50% of the economies have developed concrete actions after the proper analysis have been carried out during time. Of the economies that have surveillance programs for antimicrobial resistance in animals, only 25% have developed concrete actions after the proper analysis have been carried out during time. The main issues that prevent concrete actions from being taken or surveillance programs to be set up are:

- Lack of resources to take actions on this issue
- Lack of audit of antimicrobial use in farms and veterinary clinics

APPENDIX 1 – Survey

General Information

In the domestic context regarding the issue of antimicrobial resistance and appropriate interventions to lessen their impact, there are needs and actions that have to take place, but they must be based on knowledge.

1) List the 5 bacterial zoonotic diseases and/or foodborne diseases that represent the major challenge for public health in your economy.

1. Salmonella
2. Campylobacter
3. Listeria monocitogenes
4. E.coli

2) List the 5 bacterial infectious diseases that represent the major challenge for public health in your economy. (You are allowed to repeat from the above)

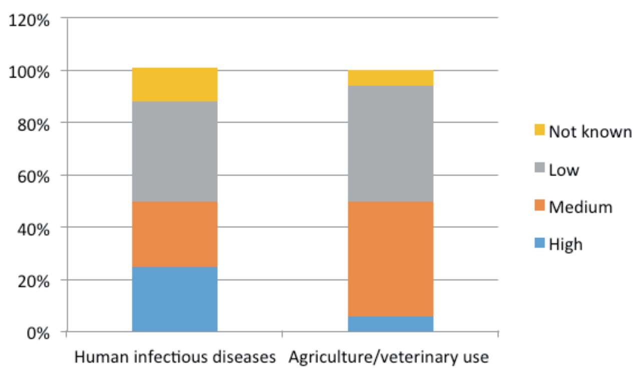
1. Salmonella
2. Tuberculosis

3) How would you describe the awareness of antimicrobial resistance in human infectious diseases in your economy?

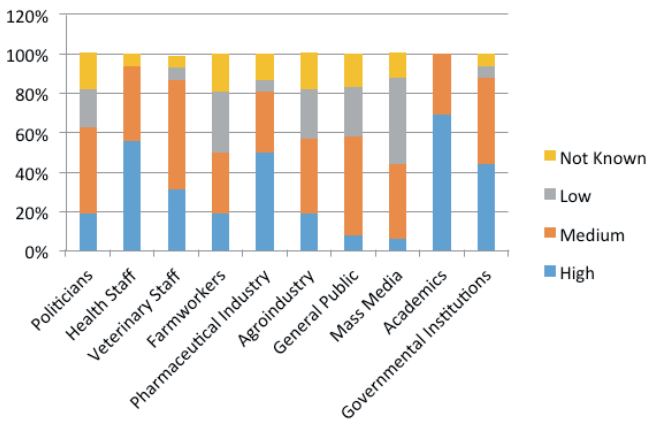
ß☐ High ß☐Medium ß☐Low ß☐None ß☐Not known

4) How would you describe the awareness of agriculture/veterinary use of antimicrobials and their contribution to AMR in human infectious diseases in your economy?

ß☐ High ß☐Medium ß☐Low ß☐None ß☐Not known

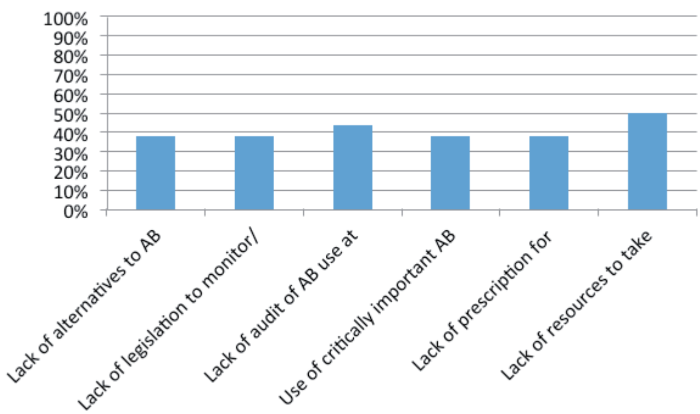


5) What would be the level of awareness in each of these different groups?



6) Of the following matters: Which ones are of most concern in addressing the issue of antimicrobial resistance in your economy?

1. Lack of Antibiotic (AB) registry
2. Lack of alternatives to AB 38%
3. Use of AB as growth promotors
4. Lack of legislation to monitor or control use of AB 38%
5. Lack of audit of AB use at farm or veterinary clinics 44%
6. Nonexistence of AMR surveillance programs (in human health)
7. Nonexistence of AMR surveillance programs (in food/animals)
8. Use of critically important AB for humans used in Agroindustry 38%
9. Lack of prescription for veterinary AB sales 38%
10. Lack of technical knowledge of AMR
11. Lack of resources to take actions on this issue 50%

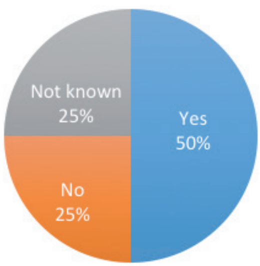


7) Does a Domestic Regulatory Authority (DRA) in charge of the registry and authorization of drugs for human use exist in your economy?
β
☐ Yes β No β Not known

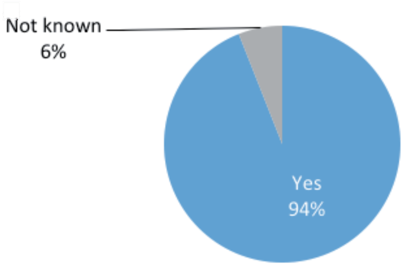
Drugs for human use: **Yes 100%**
Drugs for veterinary use: **Yes 100%**

8) Does a List of Essential Drugs (LED) exist in your economy?
β
☐ Yes β No β Not known

If it does, please include an annex or internet link to the most recent report.

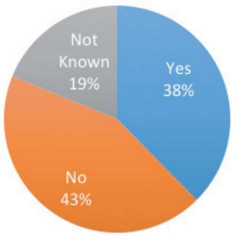


9) Does a government agency in charge of the registry and authorization of drugs for veterinary use exist in your economy?
β
Yes β No β Not known



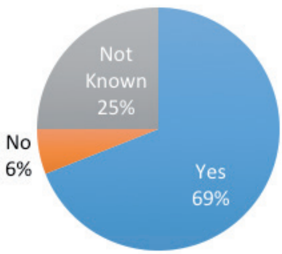
10) Does this control take place with traceability (series control throughout the food chain) program for the use of these drugs? β

☐ Yes β No β Not known

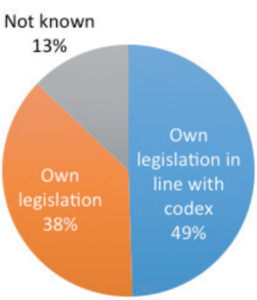


11) Does a program for the control of veterinary drug residues in food and/or the environment exist in your economy? β

☐ Yes β No β Not known

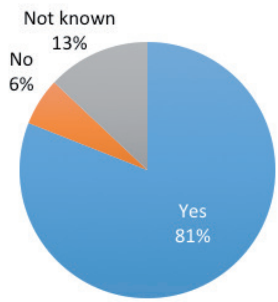


12) The list of authorized veterinary drugs in your economy corresponds to:



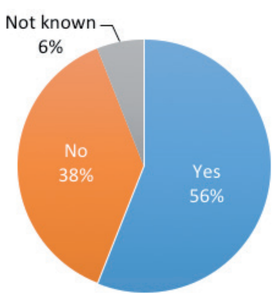
13) In your economy, do domestic standards or guidance to address AMR exist (i.e. hospital infection control, prudent use guidelines etc? β

☐Yes β☐No β☐Not known



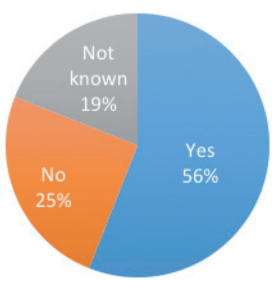
14) In your economy, by law: ¿Do AMR surveillance programs exist?

☐Yes β☐No β☐Not known

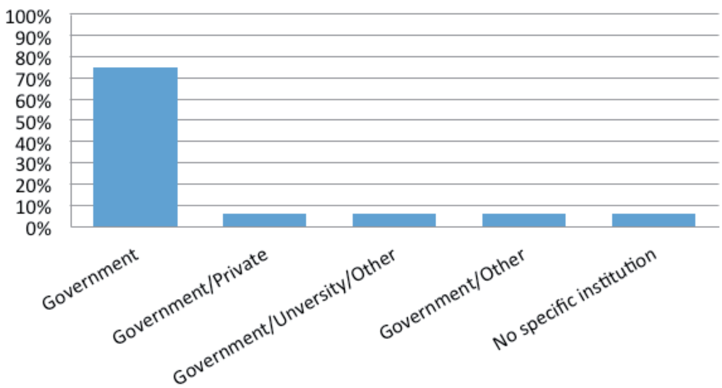


15) In your economy, do domestic standards to approach AMR exist?

☐Yes β☐No β☐Not known



17) In your economy: ¿Which institution is responsible for AMR surveillance?

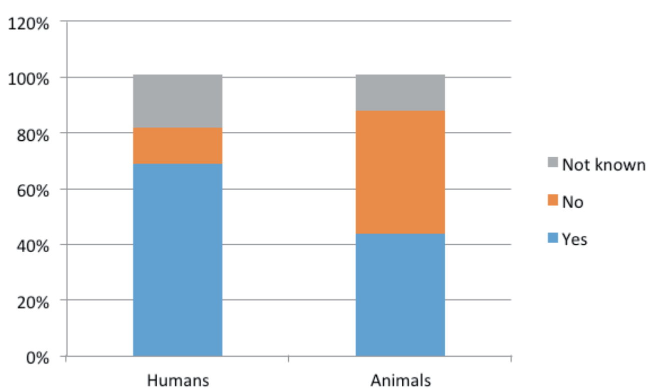


18) Does a report of epidemiological surveillance (5 years old or less) in humans exist in your economy?

☐Yes β☐No β☐Not known

20) Does a report of epidemiological surveillance (5 years old or less) on AMR in animals exist in your economy?

☐Yes β☐No β☐Not known

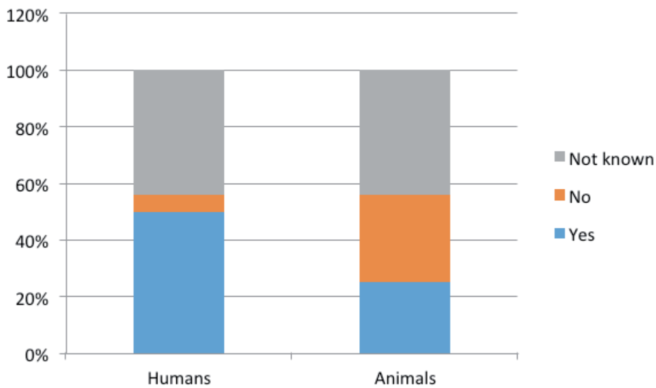


19) ¿Are concrete actions taken with the results of surveillance reports on AMR in humans?

☐Yes ß☐No ß☐Not known

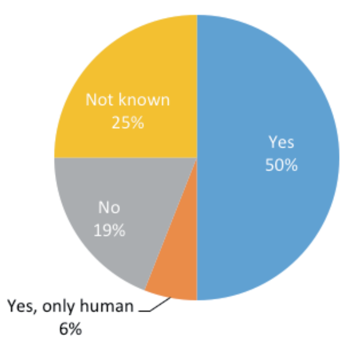
21) ¿ Are concrete actions taken with the results of surveillance reports in animals?

☐Yes ß☐No ß☐Not known

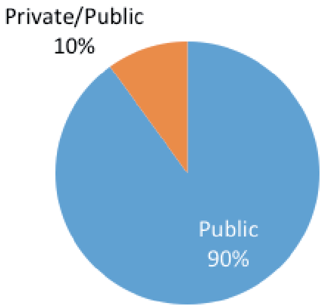


It is necessary to address the problem of antimicrobial resistance from a multisectoral perspective, integrating the vision the main areas as human health, animal and food production, in order to address the problem effectively.

22) Is there a mechanism, on a domestic level, which coordinates AMR activities in your economy?

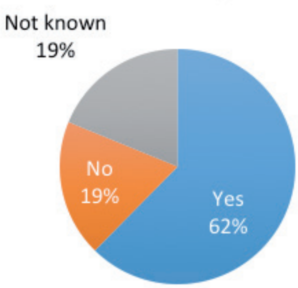


26) Does the domestic surveillance system for AMR receive any funding?
63% Yes



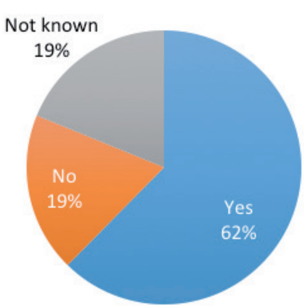
27) Does a management plan for the domestic surveillance system for AMR exist in your economy?

☐Yes β☐No β☐Not known



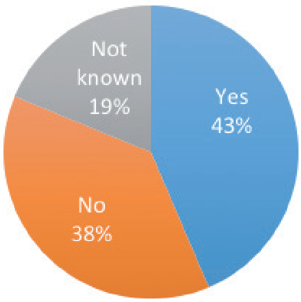
28) Is the AMR management plan active? (for ex: were there any meetings in the last year?

☐Yes β☐No β☐Not known



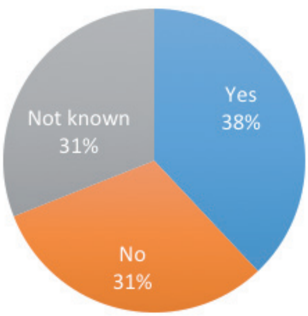
29) Does the management plan include indicators and/or goals?

☐Yes β☐No β☐Not known



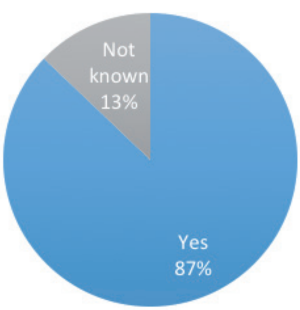
30) Is there a domestic report on AMR progress (updated in the last 5 years)?

☐Yes β☐No β☐Not known



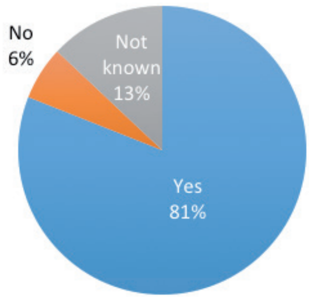
31) Is there an official Domestic Reference Laboratory (DRL) (or some other key public laboratory performing some or all of the typical tasks of DRL) for AB susceptibility testing?

☐Yes β☐No β☐Not known



32) Does the NRL (or other key laboratory) participate in a program of External Quality Assessment for antimicrobial susceptibility testing?

☐Yes ß☐No ß☐Not known



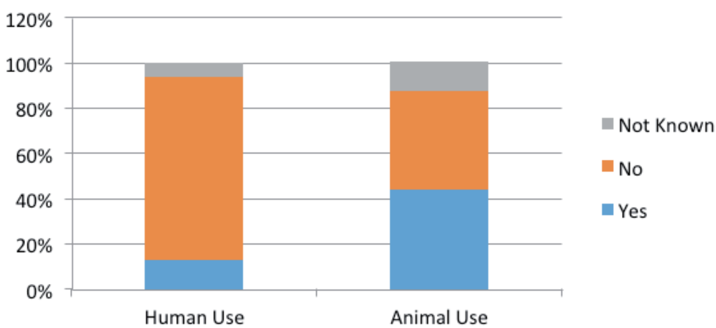
Optimal use of antimicrobials is important to minimize the emergence and spread of antimicrobial resistance and also prolongs the service life of antimicrobials.

33) Does your legislation allow the sale of antimicrobials for human use without a prescription?

☐Yes ß☐No ß☐Not known

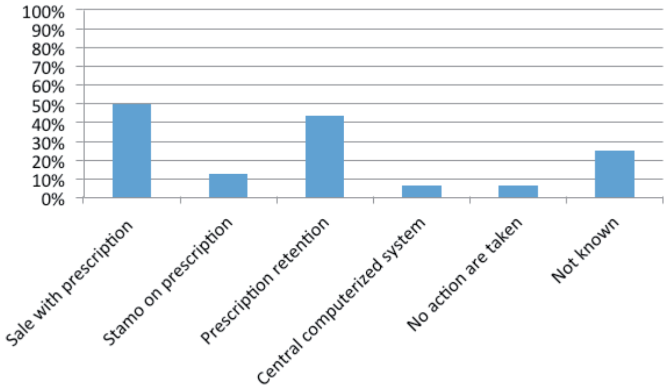
34) Does your legislation allow the sale of antimicrobials for animal use without a prescription?

☐Yes ß☐No ß☐Not known



35) If your answer is negative, what mechanisms does the Domestic Regulatory Authority use to implement the use of AB only with prescription?

☐ Sale with prescription (without stamp or retention)
☐ Stamp on the prescription (so you can't use it again)
☐ Prescription retention
☐ Central computerized system
☐ No actions are taken

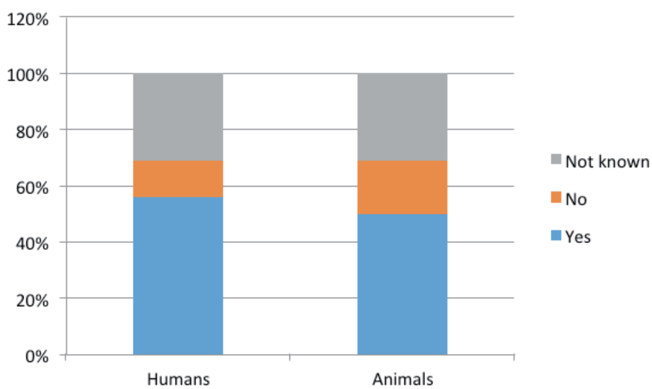


36) Have there been any public education campaigns on the correct use of antimicrobials for human use in the last two years?

☐ Yes ☐ No ☐ Not known

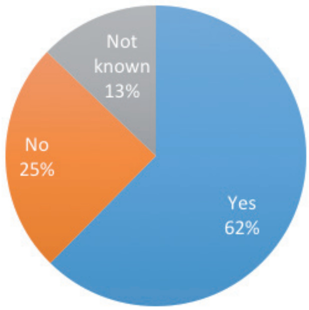
37) Have there been any public education campaigns on the correct use of antimicrobials for animal use in the last two years?

☐ Yes ☐ No ☐ Not known



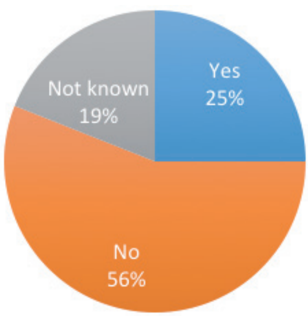
38) Is there any legislation to control the use of AB in animal husbandry?

☐Yes ꞵ☐No ꞵ☐Not known



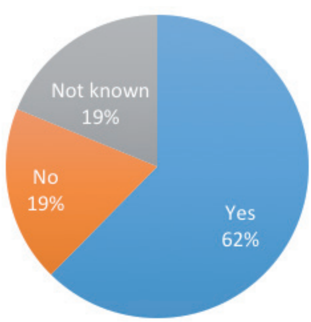
39) Are there standards for the monitoring of AMR in animal husbandry environments?

☐Yes ꞵ☐No ꞵ☐Not known



40) Does the Domestic Regulatory Authority uses any mechanism to implement the requirements for the rational use of antimicrobials in the field of animal husbandry?

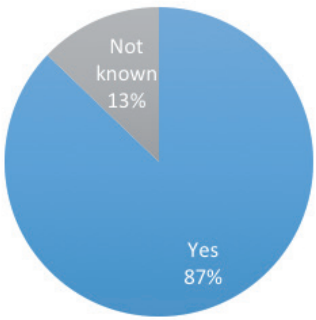
☐Yes ꞵ☐No ꞵ☐Not known



The need for antimicrobials can also be reduced with good control of infections in humans and in the veterinary field.

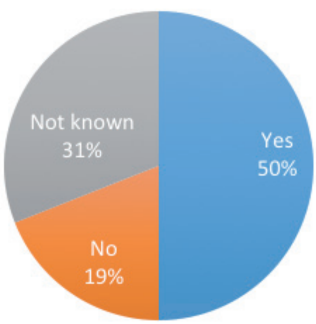
41) Is there a domestic program of mandatory reporting of infectious diseases in human patients?

☐Yes ß☐No ß☐Not known



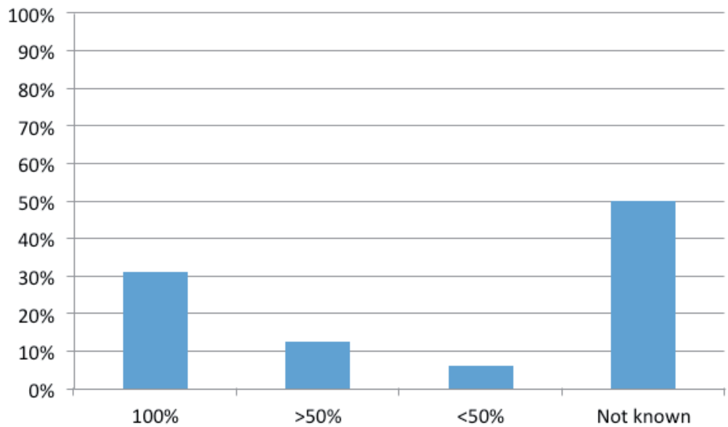
42) If you previous answer is yes, are there specific measures to control the AMR included in the mandatory reporting of infectious diseases in human patients?

☐Yes ß☐No ß☐Not known



43) What proportion of tertiary hospitals have control programs on AMR of mandatory reporting of infectious diseases in human patients?

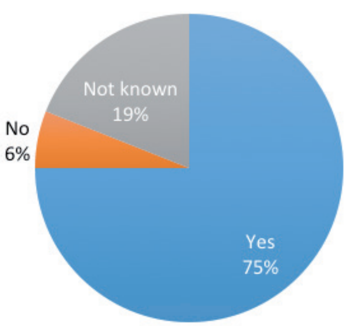
ß 100%
ß >50%
ß 50%
ß <50%
ß 0%
ß Not known



Innovation in all areas for the development of new approaches, tools and medicines are required to contain the emergence and spread of AMR.

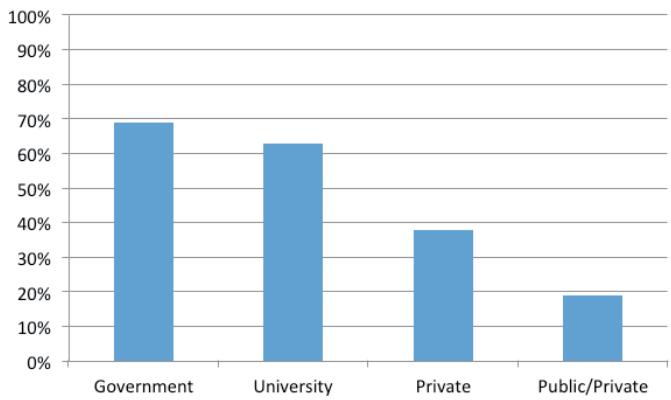
44) Is there in the economy "research and development" (R & D) related to AMR? If there is, please identify the area of R & D (i.e. epidemiological studies, assessment of resistance mechanisms).

☐Yes ßNo ßNot known



45) If your answer to the previous question is yes, which institutions carry out the research?

☐ Government 69% ☐University 63% ☐Private 38% ☐Public/Private 19%



46) Prioritize 5 actions that you consider necessary to generate an integrated AMR surveillance (humans, animals and food) plan on AMR in your economy.

1. Strengthening policies and regulations for use of AB and control program
2. Coordinate among government departments that oversee human health, animal health and food safety
3. Increased international and domestic public awareness of AMR and its implications to help engagement in the issue
4. Increase funding

APPENDIX 2 – Agenda

APEC Workshop Coordinated Research Initiative for the Implementation of Antimicrobial Resistance Control Stratregies
28–30 Oct, 2015
Santiago, Chile
AGENDA

Oct 28, 2015 Awareness

Objective: Enhance awareness, skills and knowledge in the field of AMR (focused on bacterial antimicrobial resistance), as a worldwide emerging issue in public health.

8:30 - 9:00	**Workshop Registration** **Section N°1: Workshop Presentation**
9:00 - 9:45	**Official Inauguration of the workshop** **Welcome speech** Claudio Ternecier, Undersecretary of Agriculture Andres Culagovski, Head of APEC Department, DIRECON Michel Leporati, Executive Secretary, ACHIPIA Santiago Urcelay, Dean FAVET
9:45 - 10:00	**Presentation of the project objectives** Javiera Cornejo, FAVET
10:00 - 10:30	**The Challenges and importance of Integrated AMR Surveillance** Patrick McDermott, FDA
10:30 - 10:50	**Coffee Break**
	Section N°2: The Antimicrobial Resistance Challenge
11:00 - 11:30	**Animal production role in antimicrobial resistance, AGISAR initiative** Enrique Perez, OPS
11:30 - 12:00	**OIE Standards and actions related to Antimicrobial Resistance** Martin Minassian, OIE

12:00 - 12:20	**FAO´s role and vision on AMR** Deyanira Barrero, FAO
12:20 - 12:50	**Codex approach to AMR** Rebecca Irwin, CIPARS
12:50 - 13:00	**Questions**
13:00 - 13:20	**Lunch break**
14:30 - 15:00	**WHONET and the role of laboratory-based surveillance of antimicrobial resistance at local, domestic, and global levels** John Stelling, Harvard University
15:00 - 15:40	**Antimicrobial Stewardship in veterinary medicine** Jaap Wagenaar, Utrecht University
15:40 - 16:00	**Questions**
16:00 - 16:20	**Coffee break**
16:30 - 17:00	**Antimicrobial resistance in aquaculture** Peter Smith, University of Ireland
17:00 - 17:30	**The path towards as integrated surveillance program of AMR** Enrique Perez, OPS
17:30 - 17:45	**Survey Results: Status of Integrated AMR Surveillance** Lisette Lapierre, FAVET
17:45 - 18:00	**Questions**

Oct 29, 2015 Where are we?

Objective: Strengthen technical competence of APEC economies´ representatives working in the areas related with AMR. This objective will be addressed by the lectures given by the invited experts that will participate in the workshop; these experts will provide APEC economies´ representatives with the tools to address this public health problem in order to work towards harmonized and standardized methodologies. Increase understanding of the control strategies of emergence and spread of AMR that have been used by other economies in the region and international organizations in order to improve economies' control measures and regulatory oversight of this hazard.

Session N°3: Surveillance and Monitoring Systems, Domestic and International Guidelines

8:30 – 8:45	**AMR Situation in Indonesia** Imron Suandy, Indonesia
8:45 – 9:00	**Action plans on AMR with livestock in Thailand** Mintra Lukkana, Thailand
9:00 – 9:15	**AMR Situation in Chile** Juan Carlos Hormazábal, ISP
9:15 – 9:45	**The U.S Antimicrobial Resistance Monitoring System (NARMS)** Patrick McDermott, FDA
9:45 – 10:15	**Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS)** Rebecca Irwin, CIPARS
10:15 – 10:45	**Rational use of antimicrobials in Chile** Betty San Martin, FAVET
10:45 – 11:15	**Coffee break**
11:20 – 11:40	**Colombian Integrated Program for Antimicrobial Resistance Surveillance (COIPARS)** Pilar Donado, CORPOICA
11:40 – 12:00	**Genetics and spread of antimicrobial resistance** Ricardo Castellanos Tang, Utrecht University

12:00 – 12:30	**Global survey of AMR surveillance and external quality assurance programs** John Stelling, Harvard University
12:30 – 13:00	**Interventions to reduce antimicrobial usage EFFORT: joining forces against antimicrobial resistance** Jaap Wagenaar, Utrecht University
13:00 – 13:30	**Questions**
13:30 – 14:50	**Lunch Break**
15:00 – 15:30	**Towards a risk analysis of antimicrobial use un aquaculture** Peter Smith,University of Ireland
15:30 – 16:00	**The use of whole genome sequencing for surveillance of resistance in the food chain** Patrick McDermott, FDA
16:00 – 16:15	**Coffee break**
16:20 – 16:50	**Australia´s Response to AMR and Food Safety** Steve Crossley, FSANZ
16:50 – 17:30	**From farm to fork, and across international borders: opportunities and barriers to effective intervention against antimicrobial resistance** Morgan Scott, Texas A&M University
17:30 – 18:00	**Questions**
18:00 – 20:00	**Workshop Reception for All Participants**

Oct 30, 2015 How to implement a program?

Objective: Build competency and capacity in AMR surveillance through knowledge transfer between APEC economies with ongoing surveillance programs and other developing APEC economies that do not have an ongoing surveillance program on this subject.

Section N°4: Integrated surveillance programs and the challenges for their succesful implementation

9:00 – 10:00	**Tutorial: WHONET Use and What a good platform system management must have?** John Stelling, Harvard University
10:00 – 10:15	**Working Group Session: Explanation of work methodology** Constanza Vergara, ACHIPIA
10:15 – 10:30	**Coffee break**
10:30 – 12:00	**Working Group Session** Rebecca Irwin; Patrick McDermott; Enrique Pérez
12:00 – 12:20	**Group Conclusion**
12:20 – 12:35	**Coffee break**
12:40 – 13:00	**Working Group Conclusion**
13:00 – 13:15	**Workshop Conclusions & Closure**

APPENDIX 3 – Participants

APEC Workshop Coordinated Research Initiative for the Implementation of Antimicrobial Resistance Control Strategies
28-30 Oct, 2015
Santiago, Chile
ROSTER OF PARTICIPANTS

APEC Delegates

Name	Institution
Juan Carlos Hormazábal	Public Health Institute (ISP)
Fernando Zambrano	Agriculture and Livestock Service (SAG)
Marcos Salinas	Agriculture and Livestock Service (SAG)
Alicia Gallardo	National Fisheries Service (SERNAPESCA)
Marcela Lara	National Fisheries Service (SERNAPESCA)
Fang Ying	Zhejiang entry exit inspection and Quarantine Bureau
Luo Jiyang	Chinese Academy of Inspection and Quarantine (CAIQ)
Puspita Lisdiyanti	Center for Biotechnology Research / Indonesian Institute of Sciences
Imron Suandy	Directorate Veterinary Public Health and Post Harvest, Directorate General of Livestock and Animal Health Services, Ministry of Agriculture
Susan Maphilindawati Noor	Research Center for Veterinary Science
Zawiyah Sharif	Food Safety and Quality Division/ Ministry of Health Malaysia
Jaime Oliva Rios	Federal Commission for the Protection against Sanitary Risk (COFEPRIS)
Patricia del Carmen Conde Moo	Federal Commission for the Protection against Sanitary Risk (COFEPRIS)
Farrell Benjelix Magtoto	Agriculture & Quarentine Inspection AuthorityY (NAQIA)
Elizabeth Nasing	Papua New Guinea University of Technology
Jose Carlos Silva	National Fisheries Health Agency, Ministry of Production
Maria V. Abenes	Department of Agriculture-Bureau of Animal Industry
Marissa M. Mojica	Food and Drug Administration

Vernadette S. Sanidad	National Meat Inspection Service
Mitra Lukkana	National Bureau of Agricultural Commodity and Food Standards, Ministry of Agricultural and Cooperatives
Somnuk Temvuttiroj	Division of Animal Feed and Veterinary Products Control, Department of Livestock Development, Ministry of Agriculture and Cooperatives
Kwanhatai Thongpalad	National Bureau of Agricultural Commodity and Food Standards, Ministry of Agriculture and Cooperatives
Dang Tuan Kiet	Testing Center 2 - STAMEQ
Le Thi Thuy Hang	Testing Center 1 - STAMEQ
Mai Van Tai	Research Institute for Aquaculture No. 1

Observers

Alejandra Sarquis	Interamerican Institute for Agriculture Cooperation (IICA)
Claudio Miranda	North Catholic University, Chile
Magaly Toro	University of Chile, Chile
María Margarita Jara	Central University of Chile, Chile
Fernando Zalazar	Catholic University of Valparaíso, Chile
Oscar Gallardo	National Association of Pork Product Manufacturers, Chile
Evelyn Gaete	University of Concepción, Chile
Roberto del Águila	Pan American Health Organization (PAHO)
Sandra Bravo	Austral University, Chile
Veronica García	University of Santiago, Chile
Miguel Adasme	Association of Pork Producers (ASPROCER) and Association of Poultry Producers (APA), Chile

APEC Workshop Coordinated Research Initiative for the Implementation of Antimicrobial Resistance Control Strategies v
28-30 Oct, 2015
Santiago, Chile

SPEAKERS

Dr Patrick F. McDermott

Dr. McDermott is Director of the Domestic Antimicrobial Resistance Monitoring System (NARMS) for enteric bacteria at the U.S. Food & Drug Administration (FDA). He is a Microbiologist by training, who has conducted research on antibiotic resistance for over 20 years. He is a member of the WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance (AGISAR). He represents the FDA on the U.S. government's Interagency Task Force on Antimicrobial Resistance and on the Transatlantic Task Force on Antimicrobial Resistance.

Dr Peter Smith

Based in the National University of Ireland, Galway Professor Smith has worked for 30 years on the use of antibiotics in aquaculture and has published over 80 papers on this topic. He has served as editor of the disease section of the journal Aquaculture and as chairman of the OIE ad hoc Committee on the Responsible use of Antibiotics in Aquaculture. He is a member of the Aquaculture Working Group of CSLI.

Dr Martīn S. Minassian

Dr Martin Minassian graduated as a veterinarian in 1998 from the University of Buenos Aires in Argentina; he specialized in Preventive Medicine and Public Health. Since that same year he has worked in the National Service of Agrifood Health and Quality (SENASA) as a technical supervisor of the area of registry of veterinary drugs, participating in the National Committee for residues of veterinary drugs from the International Codex Alimentarius, and acts as a coordinator of the National Special Codex group on Antimicrobial Resistance.

Since 2003, he has acted as secretary of the Committee of the Americas of Veterinary Drugs (CAMEVET), a group that is a regional representation of the OIE in the Americas.

Since 2010 he worked as technical assistant of the Regional Representation of the OIE in the Americas, participating in the support and assistance measures for the Member Economies to implement OIE standards, and the improvement of the interaction between the veterinary services, government authorities, international organizations and the private sector.

He has acted as a speaker in various events, such as in the organization and follow up work in seminars to improve the ability of veterinary services.

At the same time he has developed teaching activities at the University of Buenos Aires and union activities at the Professional Council of Veterinarians, he has also taken part in the Directive Commission of the Argentinian society of Veterinarians.

Dr John M. Stelling

Dr. Stelling, Co-Director of the WHO Collaborating Centre for Surveillance of Antimicrobial Resistance and former WHO Medical Officer, is developer of the WHONET software currently used to support local and domestic surveillance collaborations involving over 2,000 hospital, public health, food, and veterinary microbiology laboratories in over 110 economies. A priority in his work has been the translation of routinely available diagnostic laboratory information into improved clinical-decision making, public health policy, and laboratory infrastructure required for public health surveillance and research.

After his time with the Peace Corps and an MPH in biostatistics and epidemiology, Dr. Stelling began his work with WHONET during medical school, which he has continued since that time. As a Medical Officer with the World Health Organization Anti-Infective Drug Resistance Surveillance and Containment Unit, he was a coordinator of the WHO Global Strategy for Containment of Antimicrobial Resistance, and has established close working relationships with Ministries of Health and public health agencies around the world. Areas of expertise include clinical and molecular aspects of infectious diseases and antimicrobial resistance, biostatistical methods, and software development.

Dr Jaap Wagenaar

Jaap Wagenaar is expert in the field of microbiological food safety and zoonoses. He was trained as veterinarian and completed his PhD study at Utrecht University and at the USDA-Domestic Animal Diseases Center, Ames, IA, US. After obtaining his PhD degree he was appointed as Head of the Bacteriology Department of the Animal Health Service in Boxtel, the Netherlands. In 1996 he started his research group at the Institute for Animal Science and Health (currently CVI) in Lelystad, the Netherlands, on food safety and in particular on Campylobacter. Starting in 2000, Jaap Wagenaar became active in WHO-Global Foodborne Infections Network (WHO-GFN, formerly WHO-GSS), a WHO food safety program. Within that program he is member of the Steering Committee and he acts frequently as trainer in international training courses. He is director of the WHO Collaborating Center for Campylobacter and of the OIE-reference laboratory for Campylobacteriosis.

To expand his network in Public Health, he was on sabbatical leave (September 2004 - March 2006) seconded to WHO (Headquarters, Geneva, Switzerland, and for the Tsunami-relief operations to WHO Indonesia), the Centers for Disease Control and Prevention (Atlanta, US) and the USDA Western Regional Research Center (Albany, Ca, US). From 2006, Jaap Wagenaar is appointed as chair in Clinical Infectious Diseases at the Faculty of Veterinary Medicine, Utrecht University. His research group at the Vet School is focussing on Campylobacter and antimicrobial resistance. He is currently coordinator of a large EU-project on antimicrobial resistance (EFFORT). He is member of the WHO-AGISAR-group (Advisory Group on Integrated Surveillance of Antimicrobial Resistance) and member of the scientific panel of The Netherlands Veterinary Medicines Authority (SDa).

His areas of expertise are: Zoonoses, Food Safety, Food Microbiology in relation to Risk Assessment, Epidemiology of Bacterial Food Borne Diseases, Public Health, and Clinical (Veterinary) Microbiology including Antimicrobial Resistance.

Dr Rebecca Irwin

Dr Irwin received her Doctor of Veterinary Medicine degree in 1986, and a Master of Science degree in Epidemiology in 1988 from the Ontario Veterinary College, University of Guelph. Dr. Irwin has a long career with the federal government in Canada in both agriculture and health departments. Since 1998 Dr Irwin has worked intensively on the antimicrobial resistance issue and was instrumental in the founding and development of the Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS). Dr. Irwin directs the CIPARS Division, within the Centre for Food-Borne, Environmental, and Zoonotic Infectious Diseases (CFEZID), Public Health Agency of Canada. This Division operates the epidemiological aspects of AMR and AMU collection and analysis along the food chain

Dr Pilar Donado

Pilar Donado-Godoy is a Veterinarian from the National University of Colombia with a Masters Degree in Veterinary Epidemiology from the University of Guelph, Canada and a PhD in Epidemiology from the University on California, Davis. Since 1997 she works at Corpoica (Colombian Corporation of Agricultural Investigation), where in 1999 she was part of the creation of the "Quality and Safety of food of animal origin" area in this Corporation. In 2007 she started working in the implementation of the base line of antimicrobial resistance in the poultry production chain, which was the starting point for the formation of the Colombian Program for Integrated Control of Antimicrobial Resistance (COIPARS). She is a member of the WHO Advisory Group in Integrated Surveillance of Antimicrobial Resistance, AGISAR since 2014.

Dr Betty San Martin

Dr San Martin is a Veterinarian from the Austral University of Chile; she has a PhD in Veterinary Pharmacology from the Complutense University, Spain. Among her projects is the formation of FARMAVET laboratory. This is a certification lab for export products such as salmon, pork, poultry and honey, it works closely with the state and private companies, it is specialized in detecting residues of veterinary drugs and chemical contaminants in different products of animal origin, destined for export. Since 2011 it also has the Dioxin/Furan and PCBs lab. Until 2011, Dr San Martin, was a world expert for JECFA (Joint FAO/WHO Expert Committee on Food Additives). Currently she is the Coordinator of the course of "Veterinary Pharmacology" at the Faculty of Veterinary and Animal Sciences of the University of Chile, and she is the Director of the Veterinary Laboratory of Pharmacology of the Faculty of Veterinary and Animal Sciences.

Dr Morgan Scott

Dr Scott studied Veterinary Medicine at the University of Saskatchewan, he did his PhD in Epidemiology at the University of Guelph in 1998 and his Postdoc studies where in Public Health at the University of Alberta, Canada in 1999. He currently is a Professor in Epidemiology at Texas A&M University. Dr Scott studies antibiotic resistance mechanisms among foodborne pathogens and their relation with the use of antibiotics in food animals. This is a topic of increasing concern, especially where limited field data have not previously been available. In addition, Dr. Scott works to improve public health and animal well-being and to sustain healthy ecosystems by using risk analysis and epidemiologic studies to minimize the impacts of infectious hazards. Dr. Scott works closely with the livestock industry and serves as an advisor for the World Health Organization.

Mr. Stephen J. Crossley

Mr. Steve Crossley B.Sc., M.Sc., is a biochemist by training and is the manager of Scientific Strategy, International and Surveillance at Australia's domestic Food Regulator, Food Standards Australia New Zealand (FSANZ). He has 28 years' experience in food safety and risk assessment and has extensive knowledge of Codex, food surveillance, and food regulatory risk analysis. He has been an invited expert to a number of Joint FAO/WHO Meetings and Expert Consultations and has also worked for the FAO as the JECFA Joint Secretary. Prior to re-joining FSANZ in 2010, Steve worked for three years in the United Kingdom in two high profile roles: (i) leading the Scientific Evidence and Analysis program of the UK government's Food and Environment Research Agency; and (ii) as Head of Food Safety and Nutrition (Europe) of the US-based science consultancy Exponent.

Dr Enrique Perez-Gutiérrez

Senior Advisor Foodborne Diseases and Zoonosis, Department of Communicable Diseases and Health Analysis, Pan American Health Organization, World Health Organization (WHO) Washington DC, USA
Dr Perez received his DVM from the National University of Costa Rica, a Master in Preventive Medicine from the Federal University of Minas Gerais of Brazil, a Master in Veterinary Preventive Medicine from the University of California in Davis and his PhD in Epidemiology from the University of Utrecht in the Netherlands. In 2001 Dr Perez joined the Pan-American Health Organization (PAHO/WHO) responsible for providing technical cooperation in the development of risk-based, sustainable integrated food safety systems; promoting international coordination between health and agriculture sectors; and promoting and carrying out research in food safety and foodborne diseases. He is actively involved in WHO-GFN network and PulseNet Latin America and the Caribbean network. He is actively engaged in strengthening economy capacity in surveillance of foodborne diseases, burden of foodborne of diseases studies, risk assessment and antimicrobial resistance projects along the Americas.

Dr Lisette Lapierre

Dr Lisette Lapierre, Veterinary, Ph.D., assistant professor at the Faculty of Veterinary and Animal Sciences of the University of Chile since 2011. Her Ph.D. thesis was about the characterization of resistance strains of bacteria isolated from food-producing animals. She currently researches the interaction between humans, animals and the environment, bacterial foodborne diseases and antimicrobial resistance. She has been the principal researcher in 4 competitive research projects, including currently an APEC Project Coordinated Research Initiative for the Implementation of Antimicrobial Resistance Control Strategies (SCSC-FSCF). She has participated as co-researcher in 4 other projects. She has 11 ISI publications.

Dr. Michel Leporati Néron

He is a DVM from the University of Chile, PhD in Food and Environmental Resources from the Istituto Universitario Navale di Napoli, Italy, and has more than 20 years of work experience in the development of public policies for the production, research and development promotion in the agricultural sector and food industry.

He was Director of the School of Veterinary Medicine in Talca campus of Universidad Santo Tomás, Executive Director of the Plataforma de Innovación en Alimentos (PIAL) (Innovation Platform for Food) and Director of CERES-BCA services of biosecurity and food quality. He was adviser of the Ministers of Agriculture between 2006 and 2010; Vice president of the Board of Directors of the Fundación para la Innovación Agraria (FIA) (Foundation for Agricultural Innovation); Technical Secretary of the Chile: Potencia Alimentaria Public/Private Council (Chile: Power Food) and the Food Exporter Committee, among other activities.

He has developed researches and has made publications, locally and internationally, about the production, innovation and development promotion of agriculture and food sector. He has advised projects of international Cooperation through the Agencia de Cooperación de Chile (AGCI) (Chilean Cooperation International Agency) on the development of micro-to medium agri-food enterprise.

Dr. Javiera Cornejo

She has participated in different research projects related to antimicrobial resistance, residues and contaminants in food and feed. From 2005 to 2011 she worked in FARMAVET Laboratory at University of Chile, as Technical Manager responsible for the implementation and validation of the analytical methodologies and the implementation of the confirmatory dioxins laboratory. Between 2011 and 2013, she worked in the Chilean Food Quality and Safety Agency (ACHIPIA). During 2013 and 2014 she was in charge of coordinating the technical activities in Chile for the project "APEC FSCF PTIN Laboratory Competency Strengthening Initiative: Building Comprehensive Laboratory Capacity". Since August 2013, she holds the position of Assistant Professor at the Faculty of Animal and Veterinary Sciences, University of Chile, in the Food Safety Unit. From there, she directs several research projects. Currently she also is the Project Overseer of the APEC Project Coordinated

Research Initiative for the Implementation of Antimicrobial Resistance Control Strategies (SCSC-FSCF).

Deyanira Barrero

Veterinarian, specialist in epidemiology.

She has experience working in the Veterinary Service of Colombia as the Sub-manager of Livestock Protection and Regulation, and as a member of the negotiating team in Colombian Sanitary and Phytosanitary Measures (SPS) from 2005 to 2012. She is currently responsible for issues of Animal Production and Health in the Food and Agriculture Organization of the United Nations (FAO) Regional Office for Latin America and the Caribbean.

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