Tackling Foodborne Antimicrobial Resistance Globally Through Integrated Surveillance

Report of the 2nd Meeting of the WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance

5-7 June 2010

Guelph, Canada

AGISAR 2

World Health Organization

Tackling Foodborne Antimicrobial Resistance Globally Through Integrated Surveillance

Report of the 2nd Meeting of the WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance

5-7 June 2010

Guelph, Canada

AGISAR 2

World Health Organization

WHO Library Cataloguing-in-Publication Data

Report of the 2nd meeting of the WHO advisory group on integrated surveillance of antimicrobial resistance, Guelph, Canada, 5-7 June 2010.

1.Anti-infective agents - classification. 2.Anti-infective agents - adverse effects. 3.Drug resistance, microbial - drug effects. 4.Risk management. 5.Humans. I.World Health Organization.

ISBN 978 92 4 150263 4 (NLM classification: QV 250)

Printed by the WHO Document Production Services, Geneva, Switzerland.

1 Table of contents

2 Acknowledgements

The Department of Food Safety and Zoonoses, World Health Organization, Geneva, Switzerland, wishes to express its sincere thanks to all those who contributed to the success of the meeting.

We would like to thank the AGISAR members as well as the resource advisers for their valuable technical input; we are particularly grateful to Scott McEwen for outstanding chairmanship and to Carolee Carson for excellent rapporteuring.

Finally we wish to express our sincere gratitude to the University of Guelph and the Public Health Agency of Canada for hosting the meeting.

3 Preamble

The second meeting of the World Health Organization Advisory Group on Integrated Surveillance of Antimicrobial Resistance (WHO-AGISAR) was held in Guelph, Ontario, Canada, June 5-7, 2010. The meeting was convened by the World Health Organization in collaboration with the University of Guelph and the Public Health Agency of Canada.

The specific objectives of the meeting were to provide reports from the four subcommittee working groups (Data Management and Software Development, Country Pilot Projects and Capacity Building, Surveillance of Usage of Antimicrobial Agents and of Antimicrobial Resistance), including their terms of reference, future work plans or action items, and recommendations.

Following opening remarks delivered by Dr Awa Aidara-Kane, of the World Health Organization and coordinator of WHO-AGISAR, Dr Scott McEwen of the University of Guelph was elected as overall Chairperson. Dr Carolee Carson of the Public Health Agency of Canada was elected Rapporteur for the plenary, with Nicole Janecko of the Public Health Agency of Canada and Melissa Mackay and Dr Allison Mather of the University of Guelph elected Rapporteur for the subcommittee working group sessions.

The meeting was organized into three main sessions: introductory presentations; a round table discussion on emerging threats related to antimicrobial from the food-chain; and finalization of terms of reference and development of work plans by the four subcommittees.

4 Executive summary

This was the first face-to-face meeting of the four AGISAR subcommittees: (1) Data Management and Software Development, (2) Country Pilot Projects and Capacity Building, (3) Surveillance of Usage of Antimicrobial agents and (4) Surveillance of Antimicrobial Resistance. During the meeting, the experts discussed emerging threats related to antimicrobial from the food-chain and generated reports on the terms of references, action plans, and recommendations arising from the four subcommittees.

The experts expressed concern about the Emerging ESBL-producing E. coli in the community, and its association with use of cephalosporins in food animals**. *Over the last decade there continues to be a*** worldwide emerging epidemic of community-onset *E. coli* infections resistant to fluoroquinolones and 3rd generation cephalosporins. Many studies now show that a large proportion of the *E. coli* carried by people in their bowel is acquired via foods of animal origin. Poultry appears to be the major source for antibiotic resistant *E. coli* and in many countries the use of fluoroquinolones and 3rd generation cephalosporins in poultry is driving this resistance to very high levels.

AGISAR participants discussed this emerging issue and noted that higher resistance levels in people could be related to high l use of antimicrobial agents in both poultry and people; in addition the human consumption of contaminated water likely plays an important role.

Considering regional differences and challenges for implementation of integrated surveillance in different countries, AGISAR recommended that countries should start with the implementation of appropriate surveillance to obtain harmonized and standardized data from animal, food and human sectors, and then perform an integrated analysis of the data.

Finally the experts advised WHO for selection of sentinel sites to implement AGISAR pilot projects and gave valuable recommendations to the WHO regarding priorities and directions based on current AMR challenges and emerging issues.

5 Introduction

5.1 Update on WHO AMR activities and objectives of the meeting

AGISAR was first convened to be inclusive of representatives of the more advanced antimicrobial resistance (AMR) surveillance programs from around the world, with the intent to create an integrated international network of surveillance activities. After early discussions, it was decided to open the initiative to all WHO member countries, to improve effectiveness of having developing countries participate from the onset. The outcome of the first meeting in Copenhagen (2009) was to decide the strategic framework for AGISAR for the coming 5 years and undertake an updated WHO list of critically important antimicrobials for human medicine. This list is now available as a small booklet to facilitate distribution.

Recently the WHO has improved upon advocacy materials for information on foodborne AMR. For example, the WHO AMR webpage was updated to include information about Codex, AGISAR, to include the list of critically important antimicrobials, as well as information on publications and upcoming meetings.

The objectives for this 2nd meeting were to discuss emerging AMR threats from the food chain and to have the first face-to-face meeting of the four subcommittees (Data Management and Software Development, Country Pilot Projects and Capacity Building, Surveillance of Usage of Antimicrobial agents and of Antimicrobial Resistance). The expected outcome of the meeting was to generate reports on the terms of references, action plans, and recommendations arising from the four subcommittees.

6 Emerging Threats Related to Antimicrobial Resistance from the Food Chain

6.1 Emerging ESBL-producing E. coli in the community, and its association with use of cephalosporins in food animals

E. coli is the commonest cause of serious bacterial infections in people. Bloodstream infections occur at a rate of 30 to 70 episodes per 100,000 people per year in developed countries and are associated with a mortality of 10% or more. *E. coli* causes considerably more infections in other sites (e.g., urinary tract and abdomen). Infection rates are highest in the very young and old. Antibiotic resistance is a rapidly increasing problem. In some developing countries (e.g., India, China), a large proportion of *E. coli* infections may have no effective therapy available because of multi antibiotic resistance. Over the last decade there continues to be a worldwide emerging epidemic of community-onset *E. coli* infections resistant to fluoroquinolones and 3rd generation cephalosporins.

Many studies now show that a large proportion of the *E. coli* carried by people in their bowel is acquired via foods of animal origin. Poultry appears to be the major source for antibiotic resistant *E. coli*. In many countries the use of fluoroquinolones and 3rd generation cephalosporins in poultry is driving this resistance to very high levels.

The food chain is under recognised as a major source of antimicrobial resistant *E. coli*. Worldwide, much better controls are urgently needed on the use of "Critically Important" antibiotics, especially on fluoroquinolone and 3rd generation cephalosporin use in poultry.

AGISAR participants discussed this emerging issue and noted that higher resistance levels in people from the above mentioned regions could be related to high l use of antimicrobial agents in both poultry and people; in addition the human consumption of contaminated water likely plays an important role. Also, in developing countries much of the poultry production occurs in small holdings, where injectable fluoroquinolones are used, but people are also using more antimicrobials because they are less regulated. Therefore, the contribution of antimicrobial use in agriculture versus humans is difficult to unravel as the bacteria move between people and animals. In contrast, in other developing countries such as Kenya, fluoroquinolone use is banned and there is little 3rd generation cephalosporin use, thus in *E. coli* any resistance genes related to these antimicrobials are coming from humans as these antimicrobials are not used in animals. Questions were also raised about the effects of travel on AMR in human bacterial strains and whether the effects were stress-related or related to consumption of contaminated food. People are often ill soon after they travel, similar to what occurs with transporting animals and new exposures occur while travelling, with invasive disease occurring more frequently with novel exposures.

6.2 In ovo use of ceftiofur and prevalence of ceftiofur resistance among retail chicken **E. coli** *and retail chicken and human* **Salmonella** *Heidelberg in Canada*

The Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) monitors trends in antimicrobial use and resistance in bacteria from humans, animals, and meat across Canada. Canada has seen a re-emergence of resistance to the 3rd-generation cephalosporin, ceftiofur, (a critically important class of antimicrobials according to the WHO), in bacteria from abattoir and retail chicken. Ceftiofur is not labelled for use in broiler chickens and the ceftiofur label advises against extra-label use because of resistance concerns.

However, ceftiofur can legally be used in an extra-label manner under current provincial regulations, with a valid veterinarian-client-patient relationship. There is no quantitative antimicrobial use data available across years and across the country for broiler chickens.

However, a study conducted by Arsenault, Boulianne *et al*. (*in press*) indicates that 100% of the chickens from 74% of the lots slaughtered in the province of Québec (QC) between May 2003 and February 2004 had received ceftiofur in-ovo. In February 2005, following the publication of the CIPARS 2003 Annual Report which indicated a possible relationship between high prevalence of ceftiofur resistance in retail chicken and human *S.* Heidelberg, Québec hatcheries voluntarily stopped using ceftiofur in-ovo in broiler chickens. In 2007, hatcheries opted to use ceftiofur on a rotational basis with other antimicrobials (or no antimicrobials), for no longer than 6 months in a row.

CIPARS collected chicken caecal and retail meat samples from 2003 (abattoir and retail in Ontario [ON] and QC), 2005 (Saskatchewan [SK] retail), and 2007 (British Columbia [BC] retail) to 2009 (all programs/preliminary data). *E. coli*, *Salmonella*, and *Campylobacter* (retail only) were recovered. Complete sampling, bacterial isolation, serotyping, phage typing, and antimicrobial susceptibility testing methods are described in the CIPARS annual reports. Resistance breakpoints were from the Clinical Laboratory Standard Institute. Temporal changes were assessed using SAS (9.1) Chisq, or Exact statistic where appropriate. Confidence intervals were obtained using the "binomial exact" statement in PROC FREQ, using SAS (9.1).

Between the beginning of surveillance and 2009, ceftiofur resistance significantly rose in chicken abattoir *E. coli* (17% [26/153] to 29% [49/171], p=0.01) and *Salmonella* isolates (6% [8/126] to 23% [53/230], p<0.0001), and in retail SK chicken *E. coli* (4% [3/81] to 23% [21/90], p=0.0002). Ceftiofur resistance also significantly increased in 2009 compared to 2006 (last year of withdrawal) in chicken retail *E. coli* from QC (6%, 8/135, p=0.001), although it remained lower in 2009 than 2003 (33% [36/111], p=0.02). As a general rule, ceftiofur resistance is higher in BC in both retail *E. coli*

and *Salmonella.* Since the re-institution of rotational ceftiofur use, multidrug resistance in *Salmonella* isolated from chicken has remerged, with increasing prevalence of patterns such as AMC-AMP-CRO-FOX-TIO-STR-TET[1], mainly found in *S.* Kentucky.

The re-emergence of ceftiofur resistance in retail chicken *E. coli* from QC and its emergence in retail chicken from SK, the re-emergence of ceftiofur resistance in retail chicken *Salmonella* from QC and ON and high levels in BC, and similar trends observed at the national abattoir level in both *E. coli* and *Salmonella* is of considerable concern. CIPARS is actively discussing with the broiler chicken industry ways to establish a reliable drug use monitoring program.

Plenary discussions focussed on the reasons why antimicrobials, in particular ceftiofur, are used in this production stage and whether alternatives were sought by producers. Ceftiofur was used to control *E. coli* infections and related early chick mortalities as gentamicin could not longer be used because of the length of the

[1]AMC = amoxicillin-clavulanic acid; AMP = ampicillin; CRO = ceftriaxone; FOX = cefoxitin; TIO = ceftiofur; STR = streptomycin; TET = tetracycline.

gentamicin withdrawal period in light of the shortened chicken production cycle. During the period of ceftiofur withdrawal, the producers tried to use spectinomycin or nothing at all (organic) but there was little financial incentive to continue and there were no consequences for decisions affecting AMR. The producers could presently be using something else, but there is no antimicrobial use data available.

There is a lot of pressure on the industry to use ceftiofur, because neighbours are using it, competition between Québec and other provinces in Canada, importation of day-old chicks from the US that are not healthy so they are broadly treated with cephalosporins. Moreover, there is no benefit to the producer to stop using ceftiofur. The industry was unwilling to share data regarding the mortality rate decrease associated with ceftiofur use. Questions were raised about the actual dose of ceftiofur used in-ovo, as there was a suggestion that the hatcheries were under-dosing or diluting the ceftiofur and that it was not a therapeutic dose, but rather a prophylactic dose. This dilution was occurring prior to the drug being put into the in-ovo machine.

Elsewhere in the world, in Sweden, the hatcheries cover the costs of the early chick mortality up to the 5th day of life, thus there is pressure to increase the survivability of the chicks. In Australia, both fluoroquinolones and 3rd generation cephalosporins are by veterinary prescription where the extra-label use is under veterinary control. However, there is no indication of extra-label quinolone use in food animals and there does not appear to be any extra-label use in chickens.

The question was asked whether there was co-resistance detected between ESBLs and quinolones. In Canada, the resistance is primarily Amp C and there is not much quinolone resistance present yet, but it is being found in the CIPARS 2009 data using the DANMAP breakpoint. The co-resistance issues led to a discussion on the differences observed across animal species. For example, in chicken, CMY-2 is observed alone, whereas in beef cattle, CMY-2 is often linked to other antimicrobials. The plenary discussed how surveillance data is generally presented as single resistance proportions and trends are depicted using bar graphs, which would miss these differences in multidrug resistances across species. In order not to miss important findings between commodities, the raw data should be made available so that unique phenotypes can be identified.

6.3 Emerging AMR issues/challenges

The participants noted that while food-animals are one important component, there should be equal attention paid to other sectors where antimicrobials are being used, such as human medicine and companion animal medicine and that it would be remiss to not have a holistic approach, even if the focus is on a smaller section. Also, if there is too much focus on the veterinary side, this will be perceived as attributing blame to agriculture uses. There is a need to know where the resistance is coming from, and build confidence with the veterinary side to promote prudent use.

Despite the desire for a holistic approach, as AGISAR cannot focus on everything, priorities need to be established. In terms of antimicrobial use, carbapenems were identified as the most important antimicrobials, which should not be used in animals,

thus they should be the top priority for AGISAR. It is also important to highlight fluoroquinolones and 3rd/4th generation cephalosporins.

In terms of priority animal species, companion animals do not necessarily fit the focus of AGISAR. They have close contact with people, but they tend to be a closed reservoir as they are primarily an extension of the family. They do not have a lot of contact with other people, in contrast to the contact people have with food of animal origin, or the contact people have with other people. WHO recognized that it is important to consider all the reservoirs where antimicrobials are used, yet companion animals will not be a focus of AGISAR as they contribute a small proportion of resistance and priority should be on antimicrobials used in food-animals. Environmental use should also be addressed, and AGISAR might have to include advisors with competencies in this area.

In terms of priority bacterial species, multidrug-resistant *E. coli* was considered an important issue, but the question was raised whether decisions regarding bacteria for inclusion should be based on the epidemiological burden of disease. For example, should *Staphylococcus aureus* be included? MRSA is found in livestock in Canada and the US but this strain has not become much of a human health issue as of yet. The proportion of hospital based transmission versus transmission through the food-chain is unknown. In the broader scheme of MRSA issues, the livestock-associated strain appears relatively minor. MRSA might be important in Europe, but not other regions. Outbreaks of *Salmonella* and *Shigella* that are multidrug resistant should be addressed. *E. coli, Salmonella,* and *Campylobacter* should be considered in the country projects.

For analysis, molecular methods will play a role in source attribution but they should not be a priority. Regional differences and challenges for implementation of integrated surveillance in different countries should be identified.

The participants discussed whether risk management, control systems, or policy recommendations should be part of AGISAR. Advice arising from the surveillance systems should be in the framework of Codex and based on risk analysis and risk assessment, but risk management activities lay within the Codex mandate.

AGISAR should identify the minimum requirements for pilot projects and surveillance. Considerations should be regarding what is the nature of a truly integrated approach and associated recommendations for achieving this. There was a suggestion that under integrated surveillance, modeling could be used to guide the activities.

Arising from this discussion, the following are recommendations to the WHO regarding priorities and directions based on current AMR challenges and emerging issues:

1. Focus on food safety with a holistic approach
    a. How is resistance recycled to everything else, including re-exposure to both antimicrobials and resistant bacteria

2. Surveillance minimums/priorities: *E. coli*, *Salmonella*, and *Campylobacter*

a. We need to give more prominence to *E. coli*, particularly fluoroquinolone resistance and ESBLs
b. Comparison to human AMR (hospital versus community)
c. Regional differences in AMR
d. Modelling to help guide surveillance

3. What resources can we provide for developed and developing countries?
    a. Adequate surveillance systems in place at all levels (farm, abattoir, retail, humans)
    b. Consideration of inclusion of molecular level testing
    c. Advice on analysis and integration - how to standardize
    d. Use this data to help risk management - better communication to risk managers

4. AM use monitoring: Should include all antimicrobials used in people, aquaculture, horticulture, animals, including growth promoters for animals

5. Critically Important Antimicrobials: What are the priorities on this list
    a. Fluoroquinolones
    b. 3rd and 4th generation cephalosporins
    c. Carbapenems – not currently used in animals – but will be a food safety issue if carbapenem-resistant strains were in foods.

6. Effective and timely communication of emerging resistance to critically important antimicrobials within WHO and to international risk managers.

7 Background information for development of action plans and recommendations of subcommittees

7.1 Global Foodborne Infections Network country databank

GFN was previously Global *Salm*-surv with the vision that foodborne and other enteric infections are a common cause of illness, disability, and death, which can be prevented and controlled. The main activities of GFN include international training for antimicrobial susceptibility testing, epidemiology, integrated surveillance; EQAS to improve the quality of surveillance data; country databank of *Salmonella* serotypes; reference services; projects; and communication. A future endeavour would be to combine antimicrobial usage data with GFN data.

7.2 Country pilot projects and capacity-building

The focus of the subcommittee on country pilot projects and capacity-building is instituting and supporting in practice the recommendations of WHO AGISAR for surveillance of AMR and consumption. The two primary targets identified by the subcommittee as important audiences for collaboration are: 1) the existing international network of collaborators participating in GFN; and 2) pilot projects funded directly by WHO AGISAR. Priorities relevant for the Subcommittee on Data Management and Software are identified below.

Global Foodborne Infections Network

- Promote wide dissemination of software tools and protocols, and implementation by GFN members through: improved/expanded versions of WHONET and ABC Calc; training materials and tutorials; training activities and technical support.

- Promote data sharing among GFN laboratories in national, regional, and international networks.

- Strengthen and expand the GFN Country Data Bank through:
  1) standard serotype reports and electronic submissions
  2) new report formats for electronic submission of susceptibility test statistics
  3) new capacity for an isolate-level database hosted by GFN for data submitted possibly:
  -- by GFN members
  -- by authors submitting publications to the Journal of Infection in Developing Countries (JIDC)
  -- by coordinators of the WHO AGISAR-funded pilot projects

Pilot Projects

- Guidance to pilot projects with their data management strategies. In some cases, WHONET may be appropriate for managing the study data locally.

- WHONET could be used to permit harmonization and submission of final study results to the GFN Country Data Bank for integrated analysis of all pilot projects.

7.2.1 Kenya country project

The objectives of this pilot project are to describe the prevalence of *Salmonella*, *Campylobacter*, *E. coli*, and *Enterococcus* on carcasses (rectal swabs) and retail meats (raw and cooked) sold in Nairobi and Mombasa and their antimicrobial susceptibility, plus describe the antimicrobial susceptibility of enteric isolates from patients in public and private hospitals in same the study areas. The project will also study the in-vitro transferability of AMR determinants between these bacterial species isolated from food animals and meats and compare these to human data. The study is a prospective cross-sectional survey to be conducted over 12 months for the two main seasons. The study population is healthy animals (cattle, pigs, and poultry) at 8 abattoirs around Nairobi and three abattoirs from Mombasa. The retail meat isolates are collected from outlets in selected parts of the cities and the hospitals for the human isolates were selected to best represent individuals from the same abattoir distribution region. The retail meat outlets will be classified into low and high class regions according to socio-economic status. A questionnaire was developed to establish the source of the retail meat, retail practices, and farming practices. Serotyping, disc diffusion, PCR (for identification of risk factors) and PFGE (for comparison of animal and human

isolates) will be conducted. Total cost is $126,390 USD, of which WHO commitment is $80,000.

AGISAR participants discussed the pros and cons of carcass sampling and the utility of sampling cooked meat. However, the situation in Kenya is that animals are slaughtered at midnight and taken to market immediately as there is no refrigeration. Hot water is poured on them, or cold water depending on the type of slaughter house. The cooked meat is cooled off and then stored and eaten on-site.

7.2.2 China country project

China has conducted targeted surveillance activities in the past, but there is no integrated data from farm-to-table collected at the same time, or from the same area. The objectives of the pilot project are to determine the prevalence of *Salmonella*, *Campylobacter*, *E. coli*, and *Enterococcus* from farm animals, carcasses, and retail meats; to obtain representative isolates of *Salmonella* and *Shigella* from human patients; to determine the AMR patterns/genes; and to investigate the in-vitro transferability of AMR determinants in between these bacterial species. The study location is Hanzhong City and the study would be conducted over 24 months. The WHO would contribute $80,000 USD towards the study and China would contribute $70,000 USD.

As a brief summary of past AMR findings in China, in 2008 for human *Salmonella* strains, 6% were resistant to ciprofloxacin; in the Henan province, ESBL genes (CTX M9 and CTX M1) were found in *Shigella;* ESBL gene, CTX M1, was found in *Salmonella* (with resistance at very high levels for some serovars; ciprofloxacin resistance was high in human strains of *Shigella* from hospitals, and ESBLs increased in *E. coli* from inpatients between 2003 and 2005 up to 60%. For *E. coli* isolates from animals, the frequency of ciprofloxacin resistance was much higher in poultry (~50%), than swine (~20%), and higher than in humans (~15%).

AGISAR participants discussed the merits of collecting more data when some information is already available and the need for collecting data on antimicrobial use in animal populations. The plenary discussed the desire to develop the infrastructure to have integrated surveillance to identify trends occurring over time. It was noted that in some countries, the government will not invest money for sustained surveillance systems unless they are convinced it is a public health or an agriculture problem, and pilot projects such as this one can demonstrate the current situation.

7.2.3 Columbia country project

The main goal of this on-going project is to generate a baseline for the implementation of an integrated program to monitor AMR in Columbia. Objectives were to determine the prevalence, risk factors, and patterns of AMR in *Salmonella, E. coli,* and *Enterococcus* isolated from poultry farms and slaughterhouses in the most important areas of poultry production; to determine the prevalence of AMR from retail poultry meat; to compare the genetic and resistance patterns of isolates from chickens, slaughterhouses, and humans; to conduct risk assessments along the food

chain for selected pathogens; and to provide recommendations and best practices in the implementation of an integrated surveillance system on AMR. This project began in 2007.

Seventy poultry farms were enrolled (representing 12 corporations), in which farms per enterprise were selected proportionate to size. Drag swabs and pooled samples were collected. Twenty abattoirs in two regions were sampled. For retail sampling, 100 samples from distribution centres (convenience samples) were collected, plus 100 independent retail stores were sampled (30% butchers, 10% supermarkets, 60% small stores). Sampling procedures for farm and retail were based on CIPARS protocols. For humans, AMR data was collected from hospitals in the Central Region and isolates from INS in the National Region. Laboratory methods involved serotyping (Kauffman-White), PFGE, and antimicrobial susceptibility testing using the Phoenix system.

Preliminary results from the farm component showed that no antimicrobials were used for growth promotion, however, a large percentage of farms were using fluoroquinolones (25-36%). For *Salmonella*, enrofloxacin resistance was 74%; ciprofloxacin was 47%; ceftriaxone was 3%; and ceftiofur was 97%. In terms of serovars, only *S*. Heidelberg, Paratyphi B, and group 56-61 were isolated on-farm. For *Enterococcus*, resistance was reported for several antimicrobials tested (amoxicillin-clavulanic acid, mupirocin, quinupristin-dalfopristin, cefazolin, cefoxitin, clindamycin, fusidic acid, oxacillin, trimethoprim-sulfamethoxazole, gentamicin). Protective factors for AMR identified in multiple logistic regression models were disposal of dead birds by composting and cleaning of fixed equipment. Bird density per square metre was a risk factor. Drag swabs yielded higher odds of *Salmonella* isolation than fecal samples.

Preliminary results from retail indicated 25% prevalence of *Salmonella*, with more serovars identified than the farm component. For *Salmonella*, ceftiofur resistance was 94%; ciprofloxacin was 41%; and enrofloxacin was 57%. In *Enterococcus faecalis*, linezolid resistance was 1.2%. The prevalence of AMR at the farm was usually higher than retail.

Overall, the findings can contribute to policy recommendations to support biosecurity to decrease the prevalence of *Salmonella* on poultry farms; highlight the importance of assessing the classes of antimicrobials and the amounts/types used in the poultry industry; and highlight that the project needs money from AGISAR to present final result to the authorities to convene everyone and to finish with an integrated AMR surveillance system.

AGISAR participants discussed the reaction of the poultry industry to these findings. The poultry industry is collaborating with the project and they want to be competitive and to demonstrate how these problems can be addressed. Other plenary discussions arose around the comparison between ceftiofur versus ceftriaxone resistance and enrofloxacin versus levofloxacin resistance. A suggestion was made to take highest resistance rates within an antimicrobial class and use them as representative for the class and that the MIC values should be presented so that they can be interpreted with any breakpoint.

7.3 Usage Monitoring

7.3.1 The approach by the European Medicines Agency (EMA) on surveillance of antimicrobial agents in humans in Europe

Surveillance on antimicrobial usage occurs locally, nationally, regionally, and globally. Local monitoring is needed to understand and interpret AMR data. National monitoring is useful to understand the health system and interpret national levels of resistance. Cross-national studies do not provide information on how much is prescribed. For harmonization, the WHO recommends the use of ATC/vet ATC/DDD, because using the same technical unit of measurement can allow national comparisons.

European Surveillance of Antimicrobial Consumption (ESAC) has shown that it is possible to compare antimicrobial use between countries and regions. ESAC started in 2001 (ESAC I – 2001-2004) and currently includes 34 countries. ESAC's goal is to collect standardized, harmonized, and comparable data on antimicrobial consumption. For ESAC II (2004-2007), the data included outpatient and hospital data and included more drugs (antivirals, antimycotics, and antimycobacterials). ESAC III (2007-2010) includes health indicators of antimicrobial use, as well as subprojects (e.g., nursing homes) will be/were conducted. In 2010, the project will be taken over by ECDC.

Challenges and problems with collecting comparable data on antimicrobial use lie with the types of data (e.g., sales, surveys, reimbursement data); data coverage (e.g., census or sample); settings (e.g., hospitals versus nursing homes); how ATC are linked to the data (e.g., are products linked to the correct ACT code); problems with combination products; which ATC version is used; calculating DDD per package; denominators; over-the-counter drugs; or issues with inclusion of import/export/waste data. In general, ESAC data has resulted in reduced antimicrobial use in some countries, increased knowledge, and increased research on antimicrobial use. Future goals would be to have information for all species, the same methodology in each country for comparability, inclusion of cost/volume, and comparisons over time and to other nations.

Participants raised the issue that DDD are only for adult humans, although they can be used for children, the data will have to be appropriately interpreted. There is one DDD for the entire world, and the interpretation of the data is also affected if a country is using a higher dose than the DDD.

7.3.2 The EMEA approach on collection of data on use of veterinary antimicrobial agents in Europe

The European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) mandate from the Commission is to collect harmonized data on the uses of antimicrobials. The intended use of such national/community data is to aid in the interpretation of patterns and trends in AMR; to provide inputs for AMR risk profiles and risk assessments; for setting risk management priorities, for evaluation of the effectiveness of control measures being implemented; to identify emerging use of

veterinary AM agents; to aid comparison of usage of veterinary AM agents between human and veterinary medicine, time periods and countries; and as a basis for focused and targeted research and development.

EMEA has a multiphase approach involving an investigation phase (2009), pilot project (2010-2011), collecting/reporting overall national data from all member states (2011 onwards), and collecting/reporting data per species (Phase IV). Currently there are 10 countries collecting data (8 member states), and five collecting data per species. This covers over 50% of the slaughtered biomass in the member states. Challenges encountered are that not all antimicrobials included in the monitoring are reported for all countries; the data varies across nations from simple to very complex and comprehensive; the type of antimicrobial use is not always described; the data source is not always described; overall sales may be reported differently (e.g., may not be able to differentiate 3rd versus 4th generation cephalosporin use); and use per species may be reported differently.

The current project involves sales data, in which use is expressed as mg active substance sold/kg for slaughtered pigs, poultry, and cattle, plus estimated biomass of (live) dairy cattle for the corresponding year. Differences in sales relative to biomass in the 10 countries cannot be explained by differences in the animal populations alone, but may be related to differences in prescribing behaviour, animal husbandry, dosing, transport of animals to other countries for slaughter, etc. There are also differences in proportional use of different antimicrobial classes, which could be related to cost, prescribing habits, what is available on the market, etc.

A technical consultative group was established, involving the member states (including experts from countries already colleting data), ECDC, WHO, European Food Safety Authority (EFSA) and the Community Reference Laboratory (CRL), which will provide advice to EMA, such as criteria for which antimicrobials and other variables to include in the ESVAC database. For example, for each product, variables for inclusion could be country, year, Marketing Authorization Number, name, pharmaceutical form, packsize, and content unit of measurement. A pilot study was conducted using the ESVAC data collection form to gain experience for sharing this with less experienced member states. There will be a workshop to assist member states in setting up surveillance for the first time, to be held in September 2010, which is open to people/nations outside Europe to attend.

Obstacles encountered involve legal support, confidentiality issues, and the identification of the ideal data source. Next steps are to develop policies on integrated analysis of the data with AMR data in human and veterinary medicine, as well as usage in human medicine, plus further assessment of the need for legal support (i.e., pharmaceutical industry provide sales data and need for legislation to acquire data from other sources at the community level). In conclusion, the same classification should be used as human medicine (ATC/ATCvet), the collected data should be validated, DDD/animal should be the unit of measurement, and there should be representative data coverage to be able to make valid comparisons.

AGISAR plenary discussion revolved around the inclusion of WHO Euro and FAO in the project, when to include them, and that perhaps AGISAR was the global forum to share lessons learned.

8 Decisions regarding country project proposals

Decisions regarding the following country pilot proposals were presented: China, Kenya, Senegal, and Cameroon. The final rankings were that all the projects were good and met the objectives of AGISAR and that rankings mainly reflected funding limitations. Final rankings (in descending order) were China, Kenya, and Senegal. The Cameroon proposal was taken out of the country pilot program as the proposal was more focussed and the reviewers felt the proposal could use more details in areas such as methods and analysis. Additional projects requesting AGISAR support are the Columbian integrated pilot program and the processing plant sampling of swine in Costa Rica.

The FAO offered to contribute to the Kenya project as it is consistent with FAO's planned project in that region in the poultry sector. The WHO is advocating good collaborations between the three organizations (WHO, OIE, FAO), and though not encompassed in the country pilot project as of yet, poultry could be added depending on resources. The World Bank is also involved in this initiative.

9 Next steps and conclusions

The concept of integration of data was discussed; how antimicrobial use is related to AMR and how AMR is related across species. Such integration will facilitate identification and understanding of co-selection and cross-resistance issues. A suggestion was raised that data integration should be considered at the next AGISAR meeting, as this is an important gap which needs to be discussed more fully, particularly in terms of the questions "What is integration? At what levels does this occur?"

AGISAR also needs communication tools and how surveillance data can be applied to risk management, starting with voluntary options. Another subcommittee may be needed to discuss communication and how to react to information coming into the AGISAR group, and not only communicating the data to stakeholders but also the contextual problem.

In summary, issues to discuss at next AGISAR meetings are integration of data across consumption and resistance as well as across groups; data analysis in general across surveillance including issues around methodology; and communication tools and strategies. The country project proposals should be revisited, particularly by subcommittees to look for revisions on collection of use data and AMR, respectively. Perhaps, if resources allow, all the leaders (principal investigators) of the country projects could participate in a workshop on how to do the pilot project with robust methodologies.

10 ANNEX 1: Subcommittee reports

10.1 Subcommittee report: Data management and software development

10.1.1 Background

Ongoing surveillance of AMR and antimicrobial consumption is a fundamental priority established within the strategic framework developed by the WHO Advisory Committee on Integrated Surveillance of Antimicrobial Resistance (WHO AGISAR) at its first meeting in Copenhagen in 2009. To support the implementation and value of surveillance efforts, the Advisory Committee indicated that "data should be captured electronically using data management software such as WHONET or other appropriate tools".

Surveillance data are required to track evolving microbial populations, identify and respond to new and emerging threats to human and animal health, assess the qualitative and quantitative consequences of antimicrobial use practices on resistant trends, inform risk assessment and risk management investigations, guide policy, and measure the impact of interventions. WHO AGISAR aims to promote the generation and interpretation by AMR and consumption surveillance initiatives to support these aims, to facilitate standardization of such data to ensure that data are compatible so that aggregation for global analysis is possible, and to foster use of these data by policy-makers, clinicians, and other stakeholders.

Because of their existing widespread use to support surveillance initiatives and their suitability to support the recommendations of the WHO AGISAR Secretariat, the Subcommittee on Data Management and Software Development has determined that further refinement – especially for application in the food, animal, and environmental sectors – and dissemination of the WHONET (for AMR) and ABC Calc (for antimicrobial consumption) softwares would be an important step forward in fostering worldwide collaborations in integrated surveillance.

10.1.2 WHONET

The WHONET software developed by the WHO Collaborating Centre for Surveillance of Antimicrobial Resistance (Boston) is currently used to support AMR surveillance activities in over 1,300 hospital, public health, food, and veterinary laboratories in over 90 countries. The software permits flexible local customization, data entry, interactive data analysis, and standard reports. The software and accompanying tutorials are available free-of-charge from either WHO at www.who.int/drugresistance or the WHONET website at www.whonet.org.

Many laboratories in the world have electronic information systems for the storage of microbiology test results – common desktop applications (such as Microsoft Access or Excel), in-house or commercial laboratory information systems, and diagnostic laboratory instruments. The existence of such electronic data systems for laboratory

data is a rich, yet largely untapped, resource. To address the obstacle to direct data sharing posed by the use of multiple languages and incompatible data formats and codes, WHONET includes a data harmonization utility called BacLink to capture and standardize data from a variety of data sources, thereby avoiding "double data entry" into two systems, which is time-consuming, error-prone, inefficient, and de-motivating to laboratory staff, and should be avoided by all means.

Further information on WHONET and BacLink background and features can be found on the WHONET website at www.whonet.org.

10.1.3 ABC Calc

To support surveillance of statistics on antimicrobial consumption volume in human populations, the ABC Calc software – representing "Anti-Biotic Consumption Calculator" – was initially developed in France as a Microsoft Excel template and further refined at the Statens Serum Institute in Copenhagen. The system permits the entry of information on antimicrobials consumed, purchased, or dispensed and provides antimicrobials, the route of administration is also required. With the information provided, ABC Calc can return total volumes of antimicrobial used (consumed, dispensed, or purchased) categorized by ATC drug classification and presented as "Defined Daily Doses".

The ABC Calc software can be downloaded from the European Society of Clinical Microbiology and Infectious Diseases at www.escmid.org/research_projects/study_groups/esgap/abc_calc. The current ABC Calc is a Microsoft Excel template file, but development of a new more comprehensive desktop application is currently underway. Further details about ABC Calc and efforts to expand its relevance for surveillance of antimicrobial use in animas are available on the ABC Calc page of the European Society of Clinical Microbiology and Infectious Diseases at www.escmid.org/research_projects/study_groups/esgap/abc_calc.

10.1.4 Terms of reference

The Subcommittee for Data Management and Software Development will support implementation of the recommendations for data management strategies, protocols, and software tools established by the WHO AGISAR Secretariat and Subcommittees. Activities of this Subcommittee will address surveillance of resistance in microbial isolates of human, animal, food, and environmental origin and surveillance of antimicrobial consumption in human and animal populations and environmental settings.
Work of the Subcommittee will include the development, identification, and/or adaptation of softwares and data management tools which support the Secretariat recommendations for data capture, analysis, report formats, and sharing of data between WHO AGISAR collaborators. Specific activities will include:

- development of technical specifications for improving the use of WHONET for the management of resistance surveillance data for human, animal, food, and environmental microbial isolates

- development of technical specifications for improving the use of ABC Calc for the management of antimicrobial consumption statistics in human, animal, and other applications

- technical guidance on data management strategies for pilot projects funded by WHO AGISAR

- support for the expansion of surveillance activities through dissemination of WHONET and ABC Calc

- coordination with the Danish National Food Institute (DTU-Food) to improve the submission, use, and value of data submitted to the Global Foodborne Infections Network (GFN) Country Data Bank

10.1.5 Action plan

Surveillance of antimicrobial resistance

To date, the primary users of the WHONET software have been healthcare and public health professionals in hospital, community, and public health laboratories. The current software does have a number of specific features to support data management in food and animal laboratories (animal species, farm/restaurant/abattoir/*etc.* location types, food types, veterinary pathogens and antimicrobial agents, *etc.*), yet the software features relevant for data management in non-human isolates have never been formally reviewed or optimized.

To improve the suitability of WHONET to support surveillance of resistance in food, veterinary, and environmental settings, this Subcommittee has defined priority action items in two areas:

<u>Refinement of current WHONET package for use in non-human settings</u>

- Identification of public health, food, and animal laboratories which utilize WHONET for management of results from zoonotic and enteric pathogens

- Software review by WHO AGISAR committee members, current WHONET users, and other interested partners: adequacy of data fields, values, analyses, report formats, training materials, *etc.*

- Update or replacement of WHONET defaults for data fields (*e.g.* "animal species", "expiration date", "brand") relevant for microbes of food, animal, or environmental origin. This would also include fields for the results of molecular typing studies

- Update or replacement of WHONET defaults for data code lists (*e.g.* list of animal species, food and location types, specimen types)

- Addition of new analysis features, *e.g.* prevalence of microbial recovery in food products with appropriate accounting of samples with no isolates recovered (for the calculation denominator) and food samples with multiple isolates

New software directions

- Web-based data entry: As an option that may be of value to some laboratories and surveillance collaborations, web-based data entry may be advantageous. Advantages include ease of implementation (no local software installation and maintenance is required), convenience of data entry from any computer with internet-access, and off-site reliable storage of data in a secure environment (valuable for institutions with frequent issues of computer virus infection or malfunction). Advantages for multi-laboratory surveillance coordinators include immediate reporting of all results, timely feedback and mentoring of contributing laboratories, and real-time prospective detection and confirmation of importing findings and outbreaks.

- Central web-based data repositories: At present, WHONET is a desktop-oriented application with limited support for data access across the internet. National and international web-based data repositories would greatly increase the access and value of surveillance results. An early priority identified by the Subcommittee is promoting the use and expansion of the Global Foodborne Infections Network (GFN) Country Data Bank hosted by the WHO Collaborating Centre for Surveillance in Foodborne Pathogens. Specific enhancements could include:

  1) WHONET report format for reporting serotypes for batch and automated submissions to the GFN Country Data Bank;

  2) WHONET report format for submitting susceptibility test statistics to the GFN Country Data Bank, which would be a new reporting option feature for GFN; and

  3) Submission of isolate-level data to the GFN Country Data Bank. In light of recent discussions of DTU-Food staff with international collaborators, it is anticipated that submissions could come potentially from current GFN members, authors contributing publications to the Journal of Infection in Developing Countries (JIDC), and coordinators of the WHO AGISAR-funded pilot projects.

- Data confidentiality: WHONET already has a number of features for data encryption and de-identification. These would need to be reviewed and possibly expanded to meet the special needs of data sharing of results of results from food and animal isolates with close collaborators and/or a wider audience.

- Pilot projects: The data management needs of the WHO AGISAR-funded pilot projects will be reviewed, and the suitability of WHONET to support these

needs will be assessed. If identified as an important need, recommendations for feature implementation in WHONET will be established.

Surveillance of antimicrobial consumption

The Subcommittee on Antimicrobial Consumption has presented a set of data fields and values recommended as a model for data sharing of aggregate consumption statistics based on recommendations from the European Medicines Agency (EMA), the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC), and the European Surveillance of Antimicrobial Consumption (ESAC). The ABC Calc software provides a useful starting point for the capture of such data and provides an initial set of standards that could be extended and refined.

Priority items identified include:

- Coordination with ESAC coordinators on data management strategies for promoting surveillance of antimicrobial consumption both within Europe and elsewhere. As part of this, invitation to members of the ESAC coordinating body and ABC Calc development team to join the WHO AGISAR membership
- Collaborating with the ABC Calc development team in developing, implementing, and testing the beta version of the ABC Calc desktop application
- The addition of veterinary agents and corresponding ATCvet codes and DDD_{animal} definitions to ABC Calc
- The addition of relevant sampling demographics to ABC Calc indicating animal species, geographic level, type of drug statistics (consumption, purchases, dispensals, *etc.*)

This Subcommittee reviewed the protocols of pilot projects submitting for funding by WHO AGISAR to see whether there were any data management issues to address regarding antimicrobial consumption. At present, only two studies collect any information on antimicrobial use, and both in only a limited qualitative way, *e.g.* "What medicine did they use the last time animals were treated? _____". In the future, this Subcommittee will continue to review the data management needs of pilot projects and provide guidance as needed.

The focus of ABC Calc and the Subcommittee on Antimicrobial Consumption is establishing surveillance of aggregate consumption statistics highlighting the volume of antimicrobial use – "how much drug is used". The WHO AGISAR participants also discussed the value of other approaches utilizing surveys and indicator studies which address the indications, contributing factors, and appropriateness of drug use – "why are drugs used". This could be a valuable direction for WHO AGISAR to pursue in the future, but is not a priority at the present time and protocols for data collection and management were not discussed in detail.

At some point in the future, WHO AGISAR may wish to develop this type of guidance for assessing drug usage practices. At that point, a number of useful documents relevant to model have been developed and validated by the WHO

Medicines Department, the International Network for Rational Use of Drugs (INRUD), and Management Sciences for Health (MSH). These documents include: "How to Investigate the Use of Medicines by Consumers", "How to Investigate Drug Use in Health Facilities: Selected Drug Use Indicators", and "WHO Operational Package for Assessing, Monitoring, and Evaluating Country Pharmaceutical Situations". The European Surveillance has also successfully piloted a web-based "Point Prevalence Survey" using a one-day snapshot of antimicrobial use practices in participating hospitals that could also prove a useful model for emulation and expansion.

10.2 Subcommittee report: Country pilot projects and capacity building

10.2.1 Terms of reference - capacity building

Facilitate the enhancement of capacity building through GFN for the integrated surveillance of foodborne pathogens and commensal antimicrobial drug usage and AMR across sectors (animal, food, human), particularly in developing countries.

10.2.2 Action items

Action Item A

Identify and make available relevant resources of antimicrobial usage and antimicrobial integrated resistance surveillance:

- All relevant information is made available on the AGISAR website
- All tools from other subcommittees should be provided to this subcommittee
- Results from coming CABI meeting / other meetings on antimicrobial drug usage should be assessed - may be a good resource to link to under monitoring reports on the web site
- Extending the inventory on GFN web site with:
    a. Protocols / expert rules (SOP) developed by other AGISAR subcommittees.
    b. Collect monitoring reports dealing with resistance and usage.
    c. Reference strains and primer lists.
    d. Summary data of scientific papers, including monitoring data.
    e. Expert panel for data interpretation subdivided by usage and resistance.
    f. Frequently asked questions.

Action Item B

Identify potential training sites for AGISAR/GFN

- GFN terms of reference used for these sites.
- Need to choose country that has potentially large impact on global trade.
- Identify potential site for kick off meeting of integrated pilot projects.
  - Potentially may be one of the selected countries or in one of the steering committee institutes.
  - Potential training sites for implementation of the training modules:
    - Argentina and Trinidad
    - Cameroon
    - Kenya
    - Thailand
    - China
    - Poland

Action Item C

Develop and facilitate implementation of training modules for postgraduate interdisciplinary intersectoral audiences:

- Integrated surveillance of AMR, in close collaboration with the AMR monitoring subcommittee:
  - GFN protocols on identification of zoonotic and foodborne organisms, and to detect AMR.
  - Lectures and case studies on integrated surveillance.

- Raise awareness on minimal requirements for implementing integrated surveillance programs.

- Hold workshops in each country to adopt guidelines for their specific conditions.

- Develop guidelines and protocols for monitoring patterns of antimicrobial drug use, in close collaboration with the AM usage subcommittee.

- Software development and data management training, in close collaboration with the subcommittee on data management:
  - User manual for software.

- Focus detection on:
  - ESC/ carbapenemens, QNR in foodborne pathogens, commensals, Enterobacteriaceae, and Vibrionaceae.
  - Fluoroquinolone and macrolide resistance in *Campylobacter* in collaboration with the GFN lab committee:
    - Susceptibility testing/ gene detection - PCR and sequencing.
    - Need generic protocols for PCR and reference strains for emerging pathogens.

- Epidemiology training on integrated surveillance of resistance and interpretation of data through GFN Epi subcommittee:
  - Lectures on integrated surveillance and in epidemiology of AMR pathogens.
  - Cluster detection, time and space statistics.
  - Burden of disease.
  - Attribution to source of origin.
  - Risk assessment.

- Capacity to communicate AMR risk issues to appropriate audiences in collaboration with FERG Task Force of Country Protocols Policy Assessment Subcommittee:
  - Development of risk communication and advocacy lectures, tools, and materials.
  - Develop guidelines with minimal requirements for implementing integrated surveillance programs.

- Identify and engage appropriate stakeholders including policy-makers.

Action Item D

Encourage participation in external quality control systems to address proficiency/data gaps in laboratories monitoring AMR in foodborne pathogens according to FAO, WHO, OIE during AGISAR/GFN training courses. These include:

- Detect weaknesses in laboratory quality management including quality assurance protocols based on GFN/ EQAS (External Quality Assurance System) results.
- EQAS results from regions will be analyzed and low performing regions will be provided with training.
- Liaise with OIE and FAO to indentify gaps and weaknesses in veterinary laboratories.
- Review of existing data submitted to Journal of Infection in Developing Countries (JIDC) and other local journals.

10.2.3 Terms of reference - pilot projects

Facilitate pilot studies focusing on integrated surveillance of foodborne pathogens and commensals AMR, and antimicrobial drug use, with appropriate interventions in one or more developing countries.

Objectives of pilot projects

- Supplement the work of AGISAR by providing data from various parts of the world, particularly from developing countries.
- Contribute in strengthening the capacities of countries to establish their own program on integrated surveillance of AMR and antimicrobial drug use.
- Foster communication and collaboration between animal, food and health sectors, thereby contributing in better prevention and control of foodborne disease (including AMR) along the entire food chain.
- Increase awareness and commitment among countries to implement strategies for prevention and control of foodborne diseases and containment of AMR.
- Use the competency built through pilot studies to monitor effectiveness of control strategies.

General public health prerequisites include

- Capacity to recognize the public health burden due to enteric illness of a specific foodborne etiologic agent.
- Adequate infrastructure to properly collect animal, food and clinical specimens according to an appropriate scheme.
- Adequate laboratory facilities to perform antimicrobial susceptibility testing or a plan in place for transporting isolates to a reference laboratory.
- Capacities to capture, analyse, and report surveillance, and integrate other sources of information (e.g., production systems, consumption data).
- Identify potential synergies with international organizations such as FAO, OIE, WHO.

10.2.4 Action items

Identify potential country pilot sites for AGISAR

- Take into account equitable geographic distribution.
- Take into account country pilot site potential impact on global food trade.
- Political commitment.
- Endorsement of proposal by relevant stakeholders and sectors.

Assistance to design pilot projects

- AGISAR will coordinate assistance from GFN Laboratories and Epidemiology Subcommittees, WHO Collaborating Centres, and others.
- AGISAR will make available appropriate resources of existing AMR integrated surveillance systems.
- Provide adequate training as appropriate to address identified capacity gaps.
- Facilitate drafting (WR/OIE/FAO engagement) and communications.

Assist with resource mobilization for pilot projects

- Identify appropriate donors (STDF, World Bank, IDB, USAID, APEC, etc.).
- Identify technical partners.
- Make available advocacy materials.
- Engage regional FAO, WHO and OIE offices.
- Identify potential synergies between pilot projects and other ongoing existing initiatives.

Provide support as needed for project implementation and follow up, including publication of results at the national and international level

- Training and workshops in selected sites.
- Communication strategy.
- Assist in knowledge translation to policy makers.
- Assistance with data analysis and interpretation.
- Assistance in writing peer reviewed papers.
- Identify potential interventions based on the evidence.

Collaborate in achieving the sustainability of the AMR integrated surveillance system

- Technical cooperation from international organizations such as OIE, WHO, and FAO.
- Effective advocacy at all levels and dissemination of results to stakeholders.

10.2.5 Summary of recommendations

Recommendation #1: Feedback from the other WHO AGISAR subcommittees, international partners, pilot project coordinators, and other software end users should drive priorities for software development efforts of WHONET for surveillance of AMR and ABC Calc for surveillance of antimicrobial consumption.

Recommendation #2: WHO AGISAR and the Global Foodborne Infections Network should support the expansion of integrated surveillance activities in WHO Member States through dissemination, training, and support of WHONET and ABC Calc.

Recommendation #3: The WHO Collaborating Centre for Surveillance of Antimicrobial Resistance (Boston) and the WHO Collaborating Centre for Surveillance in Foodborne Pathogen (DTU-Food) should work collaboratively to strengthen and expand the data collection activities of the Global Foodborne Infection Network to include electronic and automated data submissions to the GFN Country Data Bank, including serotype, susceptibility test results, and underlying isolate-level data.

10.3 Subcommittee report: Usage monitoring

10.3.1 Terms of reference

The main aim of the subcommittee's work is to support and promote collection of standardized data on the usage of antibacterial agents for humans and animals, including aquatic species at regional/national levels. The subcommittee will explore the possible ways for supporting and promoting the collection, analyzing, and reporting of antimicrobial agents and will develop an action plan (e.g., guidelines, capacity building, etc.) to that effect.

10.3.2 Purpose of AM use surveillance

- Documentation of the situation.
- Identification of trends.
- input data for:
    - establishing associations antimicrobial usage and AMR
    - risk assessment
    - evaluation of effectiveness of interventions
    - identify need for interventions.
- Basis for focused and targeted research.
- Basis for communication.
- Proxy indicator for disease incidence.

10.3.3 Approach

- Identify the AM products on the market.
- Identify channels of AM distribution that give representative data coverage.
- What to standardize.
- Decide on which AM to be included.
- Decide which data to collect for each product.
- Decide on confidentiality politics.
- Selection of sources for population data (denominator).

As a minimum – Level 1

- Collect or estimate overall national / regional usage data on a regular basis.
- Report as weight of active substance / year (if possible by species).
- For future meetings:
    - Level 2: by species (and production type) and setting.
    - Level 3: by indication to be determined.

Level 1 Data Sources etc.

- Aggregate data:
    - Tariff declarations, pharmaceutical industry, wholesalers.

- Estimated data (AM use, species) obtained through the use of surveys, sentinel sites, insurance data:
    - For validation of aggregate data.
    - As alternative source when aggregate data from regulatory or industry sources are unavailable.

Standardization

- Common classification system – ATC/ATCvet.
- Names of active ingredient – use of ATC/ATCvet names:
    - Usually (INN names) when available, otherwise the BAN (British Approved Name) or USAN (United States Adopted Name).
- Conversion factor (WHO list).

Human Medicine – AM agents to be included as a minimum

Groups of antimicrobial agents	ATC codes
Antimicrobial agents for intestinal use (non-absorbable)	A07A
Antimicrobial agents for systemic (oral and parenteral) use	J01
Antibacterial agents used as antiparasitic agents	P01AB (Nitroimidazole derivatives)
Antimycobacterials	J04

Veterinary Medicine – AM agents to be included as a minimum

Groups of antimicrobial agents	ATCvet codes
Antimicrobial agents for intestinal use (non-absorbable)	QA07AA; QA07AB
Antimicrobial agents for systemic use	QJ01
Antimicrobial agents for intramammary use	QJ51
Antibacterial agents used as antiparasitic agents	QP51AG

Variables

- Refer to draft protocol in subcommittee report.
- Optionally, for veterinary medicine can report:
    - Species authorized.

Human and Animal Demographic Data

- Needed for derivation of numbers of humans and animals at risk.
- E.g., National or regional census data (depending on the purpose for surveillance, possibly adjusted by information from other sources).

Confidentiality of Data

- Normally, this will be addressed when the data are published at the ATC/ATCvet 3rd or 4th level of coding in annual or similar reports.
- Confidentiality policies should be developed within the country.

10.3.4 Action Plan

The action plan for monitoring AM usage at the country level will involve a series of steps according to available infrastructure.

1. Obtain consumption data by class and active substance (in tonnes) for human level and animal level. Methods of data collection may include one or both of the following:

    - To collect overall national data. Data sources may include customs, import/export data, manufacturing sales data, wholesalers, retailers, pharmacists, feed stores, feed mills and organized industry organizations.

    - Obtain consumption data by class and active substance from selected sources that can be used to extrapolate to the whole country. For human level data sources may include: surveys of hospitals and clinical pharmacies. For animal level data sources may include surveys at sentinel farms and vet pharmacies. In order to extrapolate this data on a national basis, information must be collected on the total number of hospitals, clinical pharmacies, vet pharmacies and animals by country.

2. Obtain consumption data by class and active substance stratified by animal species and by setting. For human use, setting would be stratified by hospitals, nursing homes, ambulatory clinics and pharmacies. For veterinary use species stratification would include separating into food producing animals and non-food producing animals. Settings would be stratified by farms, vet pharmacies.

    - What is used in representative region (sentinel) in surveillance in hospitals and separately in vet pharmacies.

10.4 Subcommittee report: Antimicrobial resistance monitoring

10.4.1 Background

A strategic framework was developed by the WHO Advisory Committee on Integrated Surveillance of Antimicrobial Resistance (AGISAR) on its first meeting in Copenhagen in 2009. The 2009 meeting focused on defining the minimum requirements for establishing a program of integrated surveillance in countries with limited resources. At the 2nd Meeting of AGISAR in Guelph Canada in 2010, emphasis was placed on the challenges associated with harmonising international surveillance progrograms. The need for harmonisation has been acknowledged in recommendations published from the 3rd session of the Codex *ad hoc* Intergovernmental Task Force on Antimicrobial Resistance (TFAMR): "*Methodology of surveillance programmes should be harmonized between countries"* (2), several joint expert consultations convened by the World Health Organization (WHO) (3-4), the Office International des Epizooties (OIE) (5) as well as joint consultations arranged by Food and Agriculture Organization (FAO) of the United Nations, WHO and the OIE, among others.

10.4.2 Terms of reference

- Develop recommendations for international harmonization of integrated AMR monitoring systems of food borne bacteria, including both pathogenic and commensal organisms.
- Provide guidance on surveillance and monitoring priorities and minimum requirements for integrated monitoring systems and for AGISAR pilot monitoring projects.
- Provide guidance on sampling strategies.
- Disseminate guidelines and standards on laboratory testing methods and quality assurance.
- Propose components of reporting and information sharing systems that permit regional and international comparison of findings.
- Communicate recommendations through GFN training courses, AGISAR pilot projects, and through other partnerships.

10.4.3 Purpose of antimicrobial resistance monitoring

The list below describes the major areas of consideration for monitoring of AMR in foodborne bacteria:

- Document the magnitude of the hazard.
- Detect emerging resistances in a timely manner.
- Identify trends.
- Detect the spread of resistant clones.
- Link AMR and drug use information.
- Inform risk analysis.
- Identify interventions and evaluate their effectiveness.

- Basis for focused and targeted research.
- Guide public health policy.
- Provide data for education.
- Generate reports and manage data across systems.
- Compare with usage data where possible.

10.4.4 The challenge of harmonisation

Harmonisation is the name given to the effort to replace the variety of standards and policies specific to nations with uniform global standards. Global harmonisation is occurring at all levels of enterprise, including food safety regulations (Ref.). Harmonisation does not require that all programs conduct monitoring and testing in exactly the same way. Nor is this goal practicable. Local differences in foodborne disease epidemiology, public health resources, laboratory capacity, government policies, production practices, food animal processing and distribution of food products, as well as pre-existing food safety infrastructure, all influence the design of a national monitoring program.

In the arena of AMR monitoring, the lack of harmonisation makes it difficult or impossible to compare monitoring results from different programs. Much emphasis has been place on the different criteria used to interpret data generated, whether by MIC measurements or zone diameters resulting from in vitro antimicrobial susceptibility testing. Some programs, such as EUCAST, rely on wild type cut-off values (CO_{WT}) to classify non-wild type populations as resistant. Other standards (e.g., CLSI) use clinical breakpoints, which are established using extensive data sets that incorporate pharmacological parameters, clinical outcome studies, and MIC data from wild type populations. Moreover, different clinical breakpoints and CO_{WT} values may be used in different monitoring systems. In addition, comparison of data is hampered by the use of different antimicrobial agents in the testing scheme. The goal of harmonisation is to make such disparate programs compatible with one another, or to sufficiently coincide in characteristics so that valid and consistent comparisons can be made.

Integrated monitoring of AMR in foodborne bacteria implies a program where samples are collected from humans, food animals, and food animal products destined for human consumption (OIE). How, when, and where samples are collected and processed introduce bias in monitoring. For example, research shows that the distribution of *Salmonella* serovars differs depending on sampling points in the food animal production continuum. Similary, the types of strains recovered are influenced by the laboratory methods used to cultivate bacteria from a specimen. While it may not be possible to achieve uniform global standards in this area, it is important to understand and describe the methods used, and the impact that different microbiological methods have on monitoring results.

10.4.5 Design of an integrated monitoring program

A useful monitoring program must be sustainable over time to provide the data needed for public health decision making and allocation of resources. WHO

recommends a working group to be established that includes scientists from different disciplines, as well as representatives from government agencies responsible for risk assessment and management.

The major issues that need to be addressed when establishing a monitoring system are:

1. Study population - Animal species/categories (including age) to be sampled. Food samples - abattoir vs. retail outlet, domestic vs. imported

2. Sampling plan
    a. sampling bias
    b. frequency of testing
    c. sample size
    d. sample source

3. Culture methodology
    a. limitations/biases
    b. bacterial species to be isolated
    c. storage of strains for future reference

4. In vitro antimicrobial susceptibility testing methods
    a. requirements for method to be used
    b. quality control/quality assurance testing
    c. antimicrobials to be used in susceptibility testing for *Salmonella* and *Campylobacter*

5. Reporting
    a. database design for appropriate data extraction (whonet)
    b. type of data to be reported while maintaining confidentiality
    c. analysis and interpretation of data
    d. information sharing

Sampling Design

Prioritization: For integrated surveillance, WHO recommends a three-part approach that includes bacteria from human clinical cases, raw retail meats, and food animals (Ref.).

- Where resources are limiting, the first priority is to monitor human isolates, which may be derived from institutes where laboratory capacity exists for routine clinical testing.

- Human - From health care facilities, outpatient clinics, may additionally include outbreak isolates recognizing the bias within outbreak isolates).

    - *Salmonella* from blood and stool

    - *Campylobacter* from blood and stool

- *E. coli* from blood and UTI

- There are multiple entry points for contaminants to enter the food chain. For countries that are starting surveillance programs, retail meats are the second priority for monitoring, since these represent the major route of human exposure.
    - *Salmonella, E. coli, Campylobacter*, or local priorities
- If on-farm sampling is not possible, then bacteria from healthy animals at slaughter can be used as a surrogate for resistance estimates in food animals. Intestinal contents are a more reliable source of isolates than carcass swabs. They also provide a better indication of the microbial status of an individual animal than do samples exposed to the abattoir environment.
    - Add Paula's schematic of animal sampling

Sampling representativeness

A sampling strategy should be devised to represent food production and consumption within a region. Different approaches to representative sampling design include active or passive collection of samples; random, stratified or systematically collection of samples; statistically based sampling or convenience sampling. The relative limitations of these different approaches should be known when interpreting results.

To provide an unbiased estimate of the proportion of resistance, the sampling scheme should be designed to represent national food animal production and distribution if possible.

The number of isolates collected should allow an accurate estimate of prevalence and the power to detect significant changes in resistance over time. The target isolate number will vary depending on the statistical accuracy needed to estimate prevalence and the magnitude of the changes one wishes to detect. These calculations depend on the initial prevalence of resistance in the region of study. For example, the European Food Safety Agency (EFSA) has recommended a target isolate number of 170 per year from each sampling source. This sample size is calculated to detect a change of 15% ($\pm$8%) against a backgound of 50% resistance and an increase of 5% in an environmnet with low resistance (0.1 %).

Sampling Strategy

Different information will be obtained when sampling at different points along the food production and distribution chain. It is necessary to identify mitigation and control points/interventions as each point provides data related to different entry points along the farm to fork contiuum. For example, on farm sampling is most representaive of AMR in the animal. Retail meat sampling may be closest to the

consumer but may not reflect the impact of slaughter environment on the microbial status of the sample.

It is important when reporting AMR data that the sampling strategy is described in detail in order for others to understand the interpretation of results and to enable more accurate comparisons with other monitoring programmes.

Sampling bias - It is important to recognize the bias associated with different sample sources. Research shows, for example, that salmonellae serotypes vary within an animal at different points in the production chain. Other factors affecting results include age, season, region, etc.

Frequency of testing - Sampling by consistent method should be done on a continuous or regular basis (not just point prevalence) to enable trend analysis. Frequency of testing should be driven by incident of disease under surveillance and seasonality. Many established monitoring systems collect samples monthly. Resources may not be adequate for frequent testing such as this. In such cases, a sufficient number of isolates should be collected annually for analysis.

Where resources are an issue, we cannot underemphasize that there should not be long periods of time between samplings and if sampling is reinitiated after a long period of time then it should conform to validated sampling methods to ensure comparability of results. The expectation is that sampling will occur at least annually.

Sample size - It is important that a representative sample size is tested. If this can not be done for each sample source, it is recommended that testing be limited to the most important sources associated with disease. Sample sizes should be calculated based on local prevalence data.

Sample source - recommendations for developing a new integrated monitoring system can be found in AGISAR 2009 report and the EFSA review (2008). While control programs are a good source of isolates, they represent a biased source of AMR data. Consideration must also be given to the most likely source of human contamination. Sample type varies by source and should reflect the most likely area for isolate recovery (e.g., ceca vs faeces for *Salmonella* in poultry, hide versus feces in cattle, etc). Ease of collection or cost may dictate the type of sample collected. This also includes recognition of local types of sampling, versus national or regional types of sampling. For example, the unique characteristics of open market food outlets as compared with supermarkets.

Contextual information should be collected with each sample. This may include sample type, date of collection, origin (national vs imported), drug exposure data, farm source, expiration date, travel history, etc.

Culture Methodology

Microbiological methods

The choice of microbiological culture methods is important, and the impact on laboratory results is often overlooked. It is important to understand that various recovery methods can differentially enrich for bacterial sub-populations within a sample. This can include recovery of multiple and different serovars and species, biased antimicrobial susceptibility profiles, recovery of populations harboring different virulence attributes, or selective enrichment of organisms that may not be most important in disease (REFS from Paula). As with other design considerations, culture methods should be described in detail in monitoring reports. Limitations and biases associated with culture methodology should be taken into account when comparing data between surveillance programmes.

Target organisms

Bacterial species to be included in monitoring is dependent upon regional public health priorities.

- In addition to the major foodborne pathogens, other veterinary or human bacteria (e.g., *Staphylococcus, Clostridium,* pathogenic *E. coli*), or commensal bacteria (*Enterococcus, E. coli*) might be included.

- *Salmonella* and other pathogens will not be found in all meat or animal samples. Because *E. coli* is prevalent, it can be used as a sentinel organism for AMR in Gram-negative enteric bacteria.

- We encourage monitoring laboratories to work with national reference laboratories, WHO Collaborating Centres, or other partnerships to store a representative number of isolates for further testing and data analysis.

- Bacterial should be identified to the serovar (*Salmonella*) or species (*Campylobacter*) level. If resources do not permit *Salmonella* serotyping, *E. coli* can be used to establish the infrastructure of your surveillance program and to provide a first estimate of the antimicrobial selection pressure in food production.

Standardized susceptibility testing and quality control/quality assurance

- For monitoring purposes, changes in susceptible populations are very valuable. For this reason, quantative data must be captured (MIC, zone diameters).

- Only *in vitro* antimicrobial susceptibility testing methods that have been standardized and validated under the auspices of an internationally recognized consensus standards organization (e.g., CLSI, EUCAST) can be used. These methods are official standards and cannot be modified.

- Quality control testing should follow international guidelines. QC testing is required no less than once per week.

- It is important to interpret results and categorize isolates (susceptible, intermediate, resistant, non-wild type) according to the guidelines published by the standards organization that approved the testing method used.

- Expert rules for discordant susceptibility results must be in place to assure data integrity.

- Recommended antimicrobials to test for *Salmonella* are listed in the previous AGISAR report (2009).

- Antimicrobials to test for *Campylobacter* are erythromycin and ciprofloxacin for disk diffusion. For *Campylobacter* testing by broth microdilution, QC ranges are available for: ciprofloxacin, gentamicin, clindamycin, azithromycin, erythromycin, florfenicol, nalidixic acid, and tetracycline. For agar dilution, meropenem and levofloxacin QC ranges are established.

Reporting

A major goal of harmonisation is to ensure comparability of data from different systems. Data should be presented in a format that allows application of different interpretive criteria (e.g., EUCAST epidemiological cut-off values versus CLSI clinical breakpoints).

- Dilution testing, drug dilution ranges, and MIC distribution should be reported. For disk diffution testing, zone diameters should be fully documented.

- Database needs to capture the sampling methods, including the representativeness of the sampled population in relation to the target population.

- Database design for appropriate data extraction - For ease of analysis and reporting, databases should be centered on individual isolate identifiers with links to metadata inclusive of denominator data.

- The database needs to accommodate sharing of the data while maintaining confidentiality. WHONet software is free of charge and can meet most data handling and reporting needs. This software can be customized for local monotiring purposes.

- As a public health function, monitoring results should be transparent and accessible, with a preferential option for the interests of the consumer. Once data integrity and confidentiality has been assured, data should be made freely available for independent analysis and reporting.

- Where possible, susceptibility data should be analyzed in conjunction with other available datasets such as those of Pulsenet and GFN.

- Information sharing in a format that permits regional/international comparison of antimicrobial susceptibility over time (e.g., using WHONet to capture MICs or zone sizes).

International recommendations on integrated monitoring

National AMR monitoring programs - A growing number of national monitoring programs are in place. Examples are listed in the Report of the 1st Meeting of the AGISAR in ANNEX 3. They are reproduced here for convenience.

ANNEX 3: Examples of programs on surveillance of antimicrobial resistance in animal, food, and humans

NARMS-USDA (animal) – United States
http://www.ars.usda.gov/Main/docs.htm?docid=6750&page=1
NARMS-FDA (food) – United States
http://www.fda.gov/AnimalVeterinary/SafetyHealth/AntimicrobialResistance/NationalAntimicrobialResistanceMonitoringSystem
NARMS-CDC (human) – United States
http://www.cdc.gov/NARMS
CIPARS (human, animal, food) - Canada
http://www.phac-aspc.gc.ca/cipars-picra/index-eng.php
MARAN (animal, food) - Netherlands
http://www.cvi.wur.nl/UK/publications/otherpublications/maran/
DANMAP (human, animal, food) - Denmark
http://www.danmap.org
NORM-NORMVET (human, animal, food) - Norway
http://www.vetinst.no/eng/Research/Publications/Norm-Norm-Vet-Report
EARSS (human) - 33 European countries
http://www.rivm.nl/earss/
ESAC (human usage) - 34 countries (27 EU)
http://app.esac.ua.ac.be/public/
EFSA (animal, food, human) - EU
http://www.efsa.europa.eu/
SVARM (animal) - Sweden
http://www.sva.se/en/Target-navigation/Animal-health/Antibiotic-Resistance/Monitoring-of-antimicrobialresistance/SVARM-reports/
ITAVARM (animal, human) - Italy (2003)
http://195.45.99.82:800/pdf/itavarm.pdf
MARAN (food, animal) - the Netherlands (2007)
http://www.cvi.wur.nl/NR/rdonlyres/DDA15856-1179-4CAB-BAC6-28C4728ACA03/83791/MARAN_2007_def2.pdf
FINRES-VET (animal, food) - Finland
http://www.evira.fi/uploads/WebShopFiles/1198141211941.pdf
ONERBA (animal, human) - France
http://www.onerba.org/rubrique.php3?id_rubrique=15
JVARM (animal) - Japan
http://www.maff.go.jp/nval/tyosa_kenkyu/taiseiki/monitor/e_index.html
DAFF - pilot surveillance program (animal) - Australia
http://www.daff.gov.au/agriculture-food/food/regulation-safety/antimicrobialresistance/antimicrobial_resistance_in_bacteria_of_animal_origin

11 ANNEX 2: List of participants

Barzilay, Ezra
Lead, National Surveillance Team and National Antimicrobial Resistance Monitoring System (NARMS)
Enteric Diseases Epidemiology Branch, National Center for Emerging and Zoonotic Infectious Diseases
U.S. Centers for Disease Control and Prevention
1600 Clifton Road, Mailstop D-63, Atlanta, Georgia 30329, USA
Tel: +1 404 639 3330
Fax: +1 404 718 1857
Email: Ebarzilay@cdc.gov

Blix, Hege Salvesen
WHO Collaborating Centre for Drug Statistic Methodology
Norwegian Institute of Public Health
P.O. Box 4404 Nydalen,
N-0403 Oslo, Norway
Tel: +47 21078163
Email: hege.salvesen.blix@fhi.no

Collignon, Peter
Infectious Diseases Physician and Microbiologist
Director Infectious Diseases Unit and Microbiology Department, the Canberra Hospital
Professor, School of Clinical Medicine, Australian National University
PO Box 11, Woden. ACT. 2607 Australia
Tel: +61 2 6244 2105
Fax: +61 2 6244 4646
Email : peter.collignon@act.gov.au

Fedorka Cray, Paula J.
Research Leader Bacterial Epidemiology and Antimicrobial Resistance Research Unit
Richard Russell Research Center
905 College Station Rd
Athens, GA 30605, USA
Tel: +1 706 546-3685
Fax: +1 706 546-3066
Email: paula.cray@ars.usda.gov

Grave, Kari
Norwegian School of Veterinary Science
P.O. Box 8146 Dep.
N-0033 Oslo, Norway
Tel: +47 22 96 49 88
Fax: + 47 22 96 47 52
Email address: kari.grave@veths.no

Greko, Christina
Strama VL, Dept of Animal Health and Antimicrobial Strategies
National Veterinary Institute (SVA)
SE-751 89 Uppsala, Sweden
Tel: +46 18 67 43 47
Email: christina.greko@sva.se

Irwin, Rebecca
Veterinary Epidemiologist
Director, Antimicrobial Resistance Program (VM-05)
Laboratory for Foodborne Zoonoses, Public Health Agency of Canada
R.R. # 6
Guelph, Ontario N1H 6J3
Tel: +1 519 826-2183
Email: rebecca_irwin@phac-aspc.gc.ca

Kariuki, Samuel
Centre for Microbiology Research, KEMRI
Kenyatta Hospital Compound
PO Box 43640
Nairobi - 00100, Kenya
Tel: +254-202-718247
Fax: +254-202-711673
Email: skariuki@kemri.org

Lu, Ran
Deputy director
Branch of Enteric Infection Disease Control and Prevention
Office for Disease Control and Emergency Response
Chinese Central for Disease Control and Prevention (HQ)
27 Nan Wei Lu, Beijing 100050, P. R.China
Tel/Fax: +8610-63025413
Email: ranlu66@yahoo.com / ran_lu@263.net

McDermott, Patrick
Director U.S. National Antimicrobial Resistance Monitoring System
Center for Veterinary Medicine
U.S. Food & Drug Administration
8401 Muirkirk Rd, Mod 2
Laurel, MD 20708, USA
Tel: +1 301-210-4213
Fax: +1 301-210-4298
Email: Patrick.mcdermott@fda.hhs.gov

McEwen, Scott A.
Professor & Graduate Coordinator
Department of Population Medicine
Ontario Veterinary College
University of Guelph
Guelph, Ontario, Canada
N1G 2W1
Tel: +1 519-824-4120 ext 54751
Fax: +1 519-763-3117
Email: smcewen@uoguelph.ca

Mitema, Eric
Faculty of Veterinary Medicine
Department of Public Health, Pharmacology and Toxicology
University of Nairobi
P.O. Box 29053
Nairobi, Kenya
Tel: +254 20 631277/ 630034 DL
Fax: +254 2 631325
Email: esmitema@uonbi.ac.ke

O'Brien, Tom
Co-Director
WHO Collaborating Centre for Surveillance of Antimicrobial Resistance
Brigham and Women's Hospital
Microbiology Laboratory
75 Francis Street
Boston, Massachusetts 02115, USA
Email: tobrien@rics.bwh.harvard.edu

Powers, John H.
Senior Medical Scientist
Clinical Monitoring Research Program
Support to Collaborative Clinical Research Branch (CCRB)
Division of Clinical Research (DCR)
National Institute of Allergy and Infectious Diseases (NIAID)
National Institutes of Health (NIH)
SAIC-Frederick Inc.
National Cancer Institute at Frederick
6700B Rockledge Drive
Room 1123
Bethesda, MD 20892, USA
Tel: +1 301-435-7131
Fax: +1 301-435-6739
Email: powersjohn@mail.nih.gov

Reid-Smith, Richard
Veterinary Epidemiologist
Canadian Integrated Program for Antimicrobial Resistance Surveillance
Antimicrobial Resistance Surveillance Unit
Laboratory for Foodborne Zoonoses
Public Health Agency of Canada
& Adjunct Professor
Depts. of Population Medicine & Pathobiology
University of Guelph
Public Health Agency of Canada
160 Research Lane - Unit 103
Guelph ON N1G 5B2, Canada
Tel: +1 519 826-2203
Fax: +1 519 826-2255
Email: richard_reid-smith@phac-aspc.gc.ca

Sjøgren Hendriksen, Rene
National Food Institute "DTU-Food"
Technical University of Denmark
Dept. of Microbiology and Risk Assessment
Research group on Antimicrobial Resistance and Molecular Epidemiology
Kemitorvet, Building 204ST DK-2800, Kgs. Lyngby, Denmark
Tel: +45 72346288
Fax: +45 72346001
Email: rshe@food.dtu.dk

Scott, H. Morgan
Professor, Epidemiology
Department of Diagnostic Medicine / Pathobiology
332 Coles Hall, 1600 Denison Avenue
College of Veterinary Medicine, Kansas State University
Manhattan, Kansas, 66506-5705, USA
Tel: +1-785-532-4602
Fax: +1-785-532-4851
Email: hmscott@vet.k-state.edu

Smith DeWaal, Caroline
Director, Food Safety Program
Center for Science in the Public Interest (CSPI)
1875 Connecticut Ave. NW Suite 300
Washington, D.C. 20009, USA
Tel: +1 202 777 8366
Fax: +1 202 265 4954
Email: cdewaal@cspinet.org

Stelling, John
Co-Director, WHO Collaborating Centre for Surveillance of Antimicrobial Resistance
Brigham and Women's Hospital
Microbiology Laboratory
75 Francis Street
Boston, Massachusetts 02115, USA
Email: jstelling@whonet.org

Wain, John
Head, Research and Development
Gastrointestinal, Emerging and Zoonotic Pathogens
Health Protection Agency Centre for Infections
61 Colindale Avenue
London NW9 5EQ
United Kingdom of Great Britain and Northern Ireland
Email: John.Wain@hpa.org.uk

Zaidi, Mussaret
Head, Microbiology Research Laboratory
(Jefe Laboratorio de Investigacion en Microbiologia)
Hospital General O'Horan
Av. Itzaes x Jacinto Canek
Merida, Yuc., C.P. 97000 Mexico
Tel and fax: +52-999-923-86-73
Email: mussaret_zaidi@yahoo.com

RESOURCE ADVISERS

Agerso, Yvonne
Senior Scientist
National Food Institute "DTU-Food"
Technical University of Denmark
Dept. of Microbiology and Risk Assessment
Research group on Antimicrobial Resistence and Molecular Epidemiology
Kemitorvet, Building 204ST DK-2800, Kgs. Lyngby, Denmark
Tel: +45 35886273
Email: yvoa@food.dtu.dk

Dutil, Lucie
Epidemiologist (Lead Analyst)
Laboratoire de Lutte contre les zoonoses d'origine alimentaire Agence de la santé publique du Canada
Université de Montréal Faculté de médecine vétérinaire
3200 Sicotte, C.P. 5000 St Hyacinthe (QC)
J2S 7C6 Canada
Tel: +1 450-773-8521 Ext 8614
Fax: +1 450-778-8120
Email lucie.dutil@phac-aspc.gc.ca

FAO REPRESENTATIVE

Otto, Patrick
Animal Health Officer (Veterinary Public Health)
Food and Agriculture Organization of the United Nations
Viale delle Terme di Caracalla
00153 Rome, Italy
Tel: +39 06 570 53088
Email: patrick.otto@fao.org

OIE REPRESENTATIVE

Jacques Acar
22, Rue Emeriau
75015 Paris, France
Email: jfacar7@hotmail.com / jfacar7@wanadoo.fr

Moulin, Gérard
Deputy Director of the National Agency for Veterinary medicinal products
AFSSA / ANMV
La Haute Marche
BP 90203
35302 FOUGERES, France
Tel: +33 2 99 94 78 78
Fax : +33 2 99 94 78 99
Email : g.moulin@afssa.fr

WHO SECRETARIAT

Aidara-Kane, Awa
Scientist
Department of Food Safety and Zoonoses
World Health Organization
20, Avenue Appia
1211 Geneva 27, Switzerland
Tel: +41 22 791 24 03
Fax: +41 22 791 48 07
Email: aidarakanea@who.int

Lo Fo Wong, Danilo
Scientist
Department of Food Safety and Zoonoses
World Health Organization
20, Avenue Appia
1211 Geneva 27, Switzerland
Tel. +41 22 791 3882
Email: lofowongd@who.int

Matheu, Jorge
Pan American Health Organization/World Health Organization

525, 23rd Street, NW
Washington, DC 20037, USA
Email: matheujo@paho.org

Pérez-Gutiérrez, Enrique
Health Surveillance, Disease Prevention and Control (HSD)
VPH/PANAFTOSA
Tel: +55-21-36619030
Fax: +55-21-36619027
Email: perezenr@fos.ops-oms.org / perezenr1@paho.org

12 ANNEX 3: Agenda

Time	Saturday 5 June 2010	Speaker
09.00 – 09.30	**SESSION I: Opening** • Welcome and opening remarks • Election of Chairperson • Appointment of Rapporteur • Adoption of the agenda	PHAC, Univ.Guelph., WHO
09.30-10.30	**SESSION II: Introductory Presentations** • Update on WHO AMR activities and objectives and expected outcome of the meeting • Emerging of *E. coli* with ESBL in the community, association with use of cephalosporins in food animals	Awa AIDARA-KANE Peter COLLIGNON
10.30 – 11.00	Tea/Coffee break	
11.00 - 12.30	**SESSION III: Round Table Discussion on Emerging antimicrobial threats from the food-chain.** • **Short introduction**: In ovo use of ceftiofur and prevalence of ceftiofur resistance among retail chicken *E. coli* and retail chicken and human *Salmonella* Heidelberg in Quebec, Canada • **Discussion:** What are the challenges and how they can be addressed by AGISAR 1	Lucie DUTIL Moderator : Peter COLLIGNON
12.30 – 13.30	Lunch	
13.30 – 15.30	**SESSION III: Finalization of TORs and development of work plans by subcommittees (SC)** **SC Working Groups** • Usage Monitoring • Antimicrobial Resistance Monitoring • Country Pilot projects & Capacity Building • Data Management &Software Development	
15.30 – 16.00	Coffee break	

16.00 – 17.30	**SC Working Groups** • Usage Monitoring • Antimicrobial Resistance Monitoring • Country Pilot projects & Capacity Building • Data Management &Software Development	
17.30 – 18.00	Break	
18.00 – 21.00	Working Dinner • Review of WG TORs & Discussion of significant planning issues • Group Feedback	**SC Working Groups**

Time	**Sunday, 6 June 2010**	
08.30 – 10.00	**SC Working Groups** • Usage Monitoring • Antimicrobial Resistance Monitoring • Country Pilot projects & Capacity Building • Data Management &Software Development	
10.00 – 10.30	Coffee break	
10.30 – 12.30	**PLENARY: Databank and Data Management** GFN Country Databank AGISAR Software DISCUSSION	 Danilo LO FO WONG John STELLING
12.30 – 13.30	Lunch	
13.30 – 15.30	• **PLENARY: Country Pilot projects & Focussed research projects** • Kenya Country Project • China Country Project • Columbia Country Project • DISCUSSION	 Sam KARIUKI Ran LU Enrique PEREZ
15.30 – 16.00	Coffee break	
16.00 – 17.30	**PLENARY: Usage Monitoring** The approach by EMA on surveillance of antimicrobial agents in animals in Europe Surveillance of antimicrobial agents in humans, using Europe as an example DISCUSSION	 Kari GRAVE Hege Salvesen BLIX

Time	Monday 7 June 2010	
08.30 – 10.30	**PLENARY: AMR Monitoring** Antimicrobial Resistance Monitoring: Challenges and Goals DISCUSSION: Global harmonization, AGISAR's role?	Patrick MCDERMOTT
10.30 – 11.00	Coffee break	
11.00 – 12.30	**PLENARY** **Report Finalization** **Conclusions, Next steps** **Closing remarks**	
12.30 – 13.30	Lunch	

ISBN 978 92 4 150263 4

WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance (AGISAR)
http://www.who.int/foodborne_disease/resistance/agisar/en/