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Report of the

**FAO EXPERT WORKING GROUP MEETING “SCOPING EXERCISE
TO INCREASE THE UNDERSTANDING OF RISKS OF
ANTIMICROBIAL RESISTANCE (AMR) IN AQUACULTURE”**

Palermo, Italy, 26–29 November 2018

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PREPARATION OF THIS DOCUMENT

This document presents the *Report of the FAO Expert Working Group Meeting “Scoping exercise to increase the understanding of risks of antimicrobial resistance (AMR) in aquaculture”*, which was held at the Mondello Palace Hotel, Palermo, Italy, from 26–29 November 2018. The report was prepared by Dr J. Richard Arthur (FAO Consultant, Canada) and Dr Melba B. Reantaso (Aquaculture Officer, FAO). A draft version of the report was circulated to all who participated in the expert consultation, and all relevant comments received were integrated into this final version. It is intended that this document will be circulated to interested stakeholders (i.e. competent authorities and other relevant government agencies, aquaculture producers and academia, including relevant fora) to provide information and raise awareness and build consensus on the use of risk analysis in evaluating the risks of AMR in aquaculture.

ABSTRACT

This report presents the results of an Expert Working Group Meeting convened by the Food and Agriculture Organization of the United Nations (FAO) which conducted a “Scoping exercise to increase the understanding of risks of antimicrobial resistance (AMR) in aquaculture”. The meeting was attended by 14 experts from nine countries, representing intergovernmental organizations, academia, research institutions and the private sector.

A risk profiling exercise was done on two bacterial agents important to both animal and human health, namely: *Streptococcus* spp. and *Vibrio parahaemolyticus*. These bacterial agents affect tilapia and shrimp, respectively, top aquaculture species that contribute significantly to global food and nutrition security. The risk profiling exercise for the two bacterial pathogens revealed that in both cases, the AMR risks posed by these pathogens were likely to be low and thus conducting a full risk assessment was not recommended. The risk profiling outlined in Codex Alimentarius was used as guidance, but it was recommended to review and adapt it as appropriate for aquatic AMR risk assessment.

The Expert Group agreed to develop a project proposal to contribute to a multisectoral project "Towards reducing aquaculture-based AMR through a cross-sectoral approach". The project concept note will include investigation on two bacterial agents important to both animal and human health, namely: *Streptococcus* spp. and mesophilic aeromonads.

CONTENTS

PREPARATION OF THIS DOCUMENT	iii
ABSTRACT	iv
ACKNOWLEDGEMENTS	vi
ABBREVIATIONS AND ACRONYMS.....	vii
1. BACKGROUND.....	1
1.1 Introduction.....	1
1.2 Purpose.....	2
1.3 Process	2
1.4 Participants.....	2
1.5 Products.....	2
2. SESSION 1: OPENING AND INTRODUCTIONS.....	3
2.1 Welcoming remarks and Introduction to objectives, mechanics and expectations.....	3
3. TECHNICAL PRESENTATIONS	3
3.1 Recent global and regional initiatives to reduce AMR	3
3.2 AMR in aquaculture: what do we know and what do we need to do?.....	4
3.3 CODEX Guidelines AMR risk analysis.....	5
3.4 Possible exposure pathways.....	6
3.5 Observations on the OIE RA framework and Codex framework	6
3.6 Oral delivery of medicines through aqua feed: AMR risk factors	7
3.7 The major diseases and control measures in Chinese mariculture.....	8
3.8 The preliminary investigation on AMR of common pathogenic bacteria in freshwater culture	9
3.9 Drug-resistance research on pathogenic bacteria of mariculture in YSFRI.....	9
4. SESSION 2: WORKING GROUP TASKS	10
5. SESSION 3: DISCUSSIONS ON POTENTIAL DEVELOPMENT OF A PROPOSAL TO CONTRIBUTE TO A MULTISECTORAL PROJECT	11
6. CONCLUSIONS AND WAY FORWARD.....	11
7. CLOSING REMARKS	15
8. REFERENCES	17
ANNEX 1. Draft annotated programme.....	18
ANNEX 2. List of participants.....	21
ANNEX 3. Group photographs.....	23
ANNEX 4. Example working group risk profile:	24

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The FAO gratefully acknowledges the active participation of the 14 experts to this working group meeting. The participants, who came from nine countries and represented intergovernmental organizations, academe, research institutions and the private sector are thanked for their contributions to a successful meeting and for their expressions of interest to participate in future AMR-related activities.

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This work supports FAO's Strategic Programme 4: Enable more inclusive and efficient agricultural food systems and includes and supports the pillars of the FAO Action Plan on AMR 2016–2020 (awareness, evidence, governance and practices).

ABBREVIATIONS AND ACRONYMS

AHPND	Acute hepatopancreatic necrosis disease
ALOR	Acceptable level of risk
AMR	Antimicrobial resistance
AMU	Antimicrobial use
CAC	Codex Alimentarius Commission
Cefas	Centre for Environment, Fisheries and Aquaculture Science (United Kingdom)
CLSI	Clinical & Laboratory Standards Institute
COFI/SCA	Committee on Fisheries Sub-Committee on Aquaculture (of the FAO)
ERM	Enteric red mouth disease
FAO	Food and Agriculture Organization of the United Nations
FIAA	Aquaculture Branch (of the FAO)
IRA	Import risk analysis
MBC	Minimum bactericidal concentration
MIC	Minimum inhibitory concentration
MSU	Mississippi State University
OIE	World Organisation for Animal Health (formerly Office International des Épizooties)
PCU	Population correction unit
PL	Postlarvae
PMP/AB	Progressive Management Pathway for Aquaculture Biosecurity
PRA	Pathogen risk analysis
PRFRI	Pearl River Fisheries Research Institute
RA	Risk analysis
RTCP	Regional Technical Cooperation Project (of the FAO)
RTFS	Rainbow trout fry syndrome
TTC	Red tetrazoline
UNGA	United Nations General Assembly
WHO	World Health Organization
YSFRI	Yellow Sea Fisheries Research Institute

1. BACKGROUND

1.1 Introduction

1. Since 2000, the Fisheries and Aquaculture Department of the Food and Agriculture Organization of the United Nations (FAO) has intensified efforts in understanding and applying risk analysis (RA) as a decision-making tool, especially with reference to responsible movement of live aquatic animals (FAO and NACA, 2000) and as part of a National Strategy on Aquatic Animal Health (Bondad-Reantaso *et al.*, 2008). The 2006 Joint FAO/World Organisation for Animal Health (OIE)/World Health Organization (WHO) Expert Meeting on Antimicrobial Use (AMU) and Antimicrobial Resistance (AMR) in Aquaculture identified antimicrobial residues and AMR as two important hazards. In 2008, an expert workshop organized by FAO identified the seven major risk sectors on aquaculture production (Bondad-Reantaso *et al.*, 2008), i.e. pathogen risks, food safety and public health risks, ecological (pests) risks, genetic risks, environmental risks, financial risks and social risks. Since then, FAO had been involved in activities aimed at enhancing capacities on RA for aquatic animal movements as requested by FAO Member Countries through FAO and other country or donor-funded projects. To support these activities in a systematic way, an introductory training course was developed (Arthur and Bondad-Reantaso, 2012).

2. The Global Action Plan on AMR with contributions from FAO and OIE, was adopted during the 68th World Health Assembly in May 2015 (WHO, 2015). The World Assembly of the OIE delegates in May 2015 adopted the strategy (OIE, 2016), and the 39th FAO Conference (June 2015) adopted Resolution 4/2015. A political declaration was made during a high-level meeting on AMR at the 71st United Nations General Assembly (UNGA, September 2016). The UNGA called upon the Tripartite (i.e. FAO as global leader for food and agriculture, the OIE as global leader for animal health and welfare and WHO as global leader for human health) and other intergovernmental organizations to support the development and implementation of national action plans and AMR activities at the national, regional and global levels under the One Health platform. The FAO, OIE and WHO agreed to step up joint action to combat health threats associated with interactions between humans, animals and the environment (FAO, 2018). A memorandum of understanding was signed in May 2018 to strengthen their long-standing partnership, with a strong focus on tackling AMR.

3. The FAO Action Plan on AMR 2016–2020 (FAO, 2016a, 2016b) supports the implementation of Resolution 4/2015. It addresses four major focus areas:

- *Awareness*: improve awareness on AMR and related threats
- *Evidence*: develop capacity for surveillance and monitoring of AMR and AMU in food and agriculture
- *Governance*: strengthen governance related to AMU and AMR in food and agriculture
- *Best practices*: promote good practices in food and agricultural systems and the prudent AMU

In October 2017, a Side Event (FAO, 2019) on AMR in Aquaculture was organized for the delegates participating in the FAO Committee on Fisheries Sub-Committee on Aquaculture (COFI/SCA) Ninth Session. It was a good awareness-raising event that targeted key decision-makers in the field of aquaculture. One of the highlights of the event was a consensus that awareness is a necessary first step in addressing AMR.

In view of the above background and recent developments, this FAO Expert Working Group Meeting “Scoping exercise to increase the understanding of risks of antimicrobial resistance (AMR) in aquaculture” (hereafter referred to as the “Expert Working Group Meeting”) was organized to further our understanding of AMR in the aquaculture production sector.

1.2 Purpose

The purpose of this Expert Working Group Meeting was to undertake a scoping exercise to increase our understanding on the risks of AMR in aquaculture. With the current attention given to AMR, a lot of questions and uncertainties are being raised as part of the understanding process, one of which refers to the risk of AMR in the aquaculture sector.

1.3 Process

4. As a RA for AMR has never been attempted for the aquaculture sector, in order to assess the feasibility of completing such a RA, the Expert Working Group was asked to attempt to prepare an AMR Risk Profile for a selected aquaculture system, and then, having completed this scoping exercise, to attempt to take a previously selected hazard for the selected aquaculture system through the major technical portions of the RA process (i.e. risk assessment and risk management (risk evaluation)) as outlined in the OIE's *Aquatic Animal Health Code, 2018* (OIE, 2018) and using a qualitative RA approach. By undertaking this exercise, it was hoped that the Expert Working Group would be able to determine whether RA is a tool that has practical application for evaluating hazards associated with AMR in aquaculture, determining if an identified hazard poses a significant risk to aquaculture and/or human society, and if so, identifying ways to reduce the risk to an acceptable level. The Expert Working Group was to look at the various steps in the RA process as outlined by the OIE's *Aquatic Animal Health Code, 2018* (OIE, 2018) and Codex Alimentarius Commission (CAC) guidelines CAC/GL 77-2011 (CAC, 2011) to see if adequate information is available to allow calculation of a risk estimate, to identify any areas of the RA process where difficulties are likely to occur, and to suggest ways of dealing with these problem areas. The Expert Working Group was also to look briefly at the possibility of preparing a proposal for a multisectoral (aquaculture, livestock, human medicine) AMR RA, including a justification, approach, possible participants and potential funding agencies.

5. To assist with these efforts, some information documents were prepared prior to the meeting and communicated to participating experts and a list of key documents (and access urls) to be used during the meeting was provided.

1.4 Participants

6. The Expert Working Group Meeting was held at the Mondello Palace Hotel, Palermo, Italy from 26–29 November 2018. A total of 14 experts coming from nine countries participated in the meeting. The list of participants and group photographs can be found in Annexes 2 and 3, respectively.

1.5 Products

7. The following were the expected outputs of the Expert Working Group Meeting:

- Risk profile for a selected aquaculture system
- Results of an attempted AMR RA (until risk evaluation), using the OIE RA framework, including identification of possible problems (information gaps, etc.) and recommendations
- Framework for a proposal for multisectoral AMR RA
- Recommendations for future Expert Working Group actions
- Report of the Expert Working Group Meeting (this document)

8. It was recognized that the approach outlined above, and in the draft programme (Annex 1), as well as the hoped for products, might not be achievable and were likely to be modified by the Expert Working Group. This proved to be the case, new agendas being prepared for each day of the meeting based on the recommendations and decisions made by the experts.

2. SESSION 1: OPENING AND INTRODUCTIONS

2.1 Welcoming remarks and Introduction to objectives, mechanics and expectations

9. The participants were welcomed by Dr Melba Reantaso (FAO, Rome) on behalf of the FAO, who stressed the informal nature of the meeting and wished them a successful discussion and a pleasant stay in Palermo.

10. She then briefly presented the meeting's 4 Ps: Purpose, Process, Participants, and Products. These are as outlined in Sections 1.2 to 1.5 of this report.

3. TECHNICAL PRESENTATIONS

11. To provide background information and set the tone for the Expert Working Group Meeting, nine technical presentations then followed during Session 1 on Days 1 and 2. Summaries of these presentations are given below.

3.1 Recent global and regional initiatives to reduce AMR

(Dr Melba B. Reantaso, FAO, Rome)

12. Dr Reantaso began her talk by presenting the most recent FAO fisheries and aquaculture statistics. She highlighted that in 2016, world aquaculture production accounted for 46.5 percent of total production (including for non-food uses) from capture fisheries and aquaculture, up from 44.7 percent in 2014, 25.8 percent in 2000 and 7.3 percent in 1980. She then presented value and volume production data for the top-12 aquaculture producers, these being, in descending order, the People's Republic of China, India, Indonesia, Viet Nam, Bangladesh, Egypt, Norway, Chile, Myanmar, Thailand, the Philippines and Japan. After discussing the complex nature of aquaculture, in terms of the large number of species cultured and the variety of culture systems, she then briefly reviewed the history of some of the major disease outbreaks affecting the sector and gave details of the chronology the emergence of some of the major shrimp pathogens from the 1970s to the present. Dr Reantaso then touched on the drivers of disease emergence, which she listed as: (i) trade in live aquatic animals, (ii) ecosystem change, (iii) lack of knowledge of the pathogens and their hosts, and (iv) weaknesses in aquatic animal health management and disease control.

13. She then turned to recent initiatives in preventing AMR, noting that this is not a stand-alone issue. These included the 68th World Health Assembly (May 2015), at which the Global Action Plan on AMR was adopted (with contributions by FAO and OIE); the 83rd World Assembly of the OIE Delegates (May 2015), which adopted Resolution No. 26 on AMR; the 39th FAO Conference (June 2015), which adopted Resolution 4/2015 on AMR; and the 71st UNGA – High Level Meeting on AMR (September 2016), with an associated Political Declaration. UNGA called upon the Tripartite (FAO, OIE and WHO) and other intergovernmental organizations to support the development and implementation of national action plans and AMR activities at the national, regional and global levels. She then pointed out the very complex interface surrounding AMR, with at least 14 different production systems and sectors involved, operating in both the aquatic and terrestrial environments. At FAO, One Health is being addressed by an Interdepartmental Working Group having the multidisciplinary expertise needed to address a cross-sectoral issue such as AMR (i.e. animal health, livestock and production, food and feed safety, plant health and production, fisheries and aquaculture, legislative contexts, etc.). Each of these aspects was considered in developing the FAO Action Plan (in support of the Global Action Plan on AMR) and its implementation at the national and regional levels. She then went on to briefly mention the many areas of FAO advocacy and tools in aquaculture biosecurity and AMR. These include the many FAO meetings, workshops and publications dealing with the issues of AMR and aquatic biosecurity. She noted that aquaculture biosecurity (including AMR) is being proposed as an agenda item during the Tenth Session of COFI/SCA, which will be held in August 2019

in Norway. Finally, she reviewed the most important bacterial diseases affecting aquaculture based on the economic importance of affected species, their socio-economic impacts and their zoonotic potential. She then closed by giving some preliminary results from FAO-funded AMU/AMR surveys conducted in the Malaysia, Philippines and Viet Nam.

3.2 AMR in aquaculture: what do we know and what do we need to do?

(Dr David Verner-Jeffreys, Centre for Environment, Fisheries and Aquaculture Science (Cefas) Weymouth Laboratory, United Kingdom)

14. Dr Verner-Jeffreys began his presentation by discussing what is AMR and the various means by which it arises. He noted a statement from a recent publication that “We estimate that by 2050, 10 million lives a year and a cumulative USD 100 trillion of economic output are at risk due to the rise of drug resistant infections if we do not find proactive solutions now to slow down the rise of drug resistance.” He then noted the slowdown in the discovery of new drugs against bacterial infections, and that AMR must be tackled on ten fronts. In the United Kingdom, the Veterinary Medicines Directorate collects antibiotic sales data from pharmaceutical companies and this is reported annually. Antibiotics sales are then reported as an “mg/PCU”, where PCU (population correction unit) is a kg figure that represents the average weight of all livestock at time of treatment. The overall sales of antibiotics for use in livestock decreased by 10 percent between 2014 and 2015, from 62 mg/PCU to 56 mg/PCU. This means there is good progress towards the government target of achieving 50 mg/kg by 2018. The European Medicines Agency categorizes the following as “Highest Priority” according to degree of risk in man due to resistance developing following use in animals: fluoroquinolones, third and fourth generation cephalosporins and colistin. In the United Kingdom, highest priority critically important antibiotics represent only a small percentage of antibiotics used. He noted that one limitation of sales data is that many products are licensed for multiple species, so it is not possible to accurately determine usage by species sector from sales data alone. In addition, some products are used “off license” in other species under the cascade. In aquaculture, antimicrobials are used to control bacterial diseases in farmed fish. In the United Kingdom, there is a limited range of available licensed antibiotics: oxytetracycline, amoxicillin (oxolinic acid) and florfenicol. Vaccines have reduced use in some countries, e.g. from 50 tonnes in Norway in 1991 to 649 kg in 2007. Early reports of resistance appeared in North America, for SA and Tet resistant *Aeromonas salmonicida* strains in the 1950s and 1960s, and pentaresistant strains by the early 1990s in North European Atlantic salmon culture. He stated that some resistance is intrinsic (e.g. to quinolones). There was early recognition of the role of conjugative plasmids in spreading AMR in aquaculture pathogens. R plasmids are now found in almost all drug-resistant fish pathogens, and there is increasing evidence that these R plasmids, and associated AMR genes, integrons and transposons, are often very similar to those found in clinical isolates. He then posed the question “Could the aquatic environment be acting as a mixing pot that facilitates AMR emergence and spread?” and examined the complex connections between human populations, the terrestrial environment and aquatic systems. Regarding the drivers of AMR in aquaculture systems, there is direct selection pressure linked to AMU and gene transfer from the environment (via pond fertilization, agricultural runoff and human effluents). He then provided detailed information on AMR in a number of species and aquaculture systems: ampicillin resistance in *A. salmonicida*, IncA/C (a group of plasmids conferring resistance to a range of antibiotics, including florfenicol, streptomycin and tetracycline that are now found in numerous distantly related bacteria), and ornamental fish. Dr Verner-Jeffreys then highlighted various aspects of Section 6 of the OIE *Aquatic Animal Health Code* (OIE, 2018), which deals with AMU in aquatic animals. He then presented details of several AMR surveillance programmes, including for *Salmonella* and *Flavobacterium psychrophilum* (rainbow trout fry syndrome (RTFS)/bacterial coldwater disease). He concluded that the AMU in aquaculture has driven selection of resistant bacteria. There is strong evidence for the transfer of R determinants and plasmids from human/terrestrial animal environments into aquaculture environments (*E. coli*, *Salmonella*, *Pseudomonas*); however, transfer in the opposite direction has yet to be established. The focus of future work should be on: (i) determining the extent of AMU in aquaculture; (ii) assessing development of resistance in key pathogens; (iii) gaining a better understanding of factors promoting environmental persistence (e.g. co-selection

for metals/biocide resistance); (iv) assessing the real risks to humans and fish of AMU in aquaculture; and (v) recommending methods and practices to minimize identified risks. One Health approaches are needed!

3.3 CODEX Guidelines AMR risk analysis

(Dr Iddya Karunasagar, FAO Expert, India)

15. Dr Karunasagar provided the participants with an in-depth presentation of the Joint FAO/ WHO CAC procedures for microbiological risk assessment as detailed in the publications *Principles and Guidelines for the Conduct of Microbiological Risk Assessment CAC/GL 30-1999* (CAC, 1999) and *Guidelines for Risk Analysis for Foodborne Microbiological Resistance CAC/GL 77-2011* (CAC, 2011). He first provided the basic structure for RA (Risk Assessment, Risk Management, Risk Communication) and a generic framework for the RA process. The first step in determining if an RA is needed is the preparation of a Risk Profile. He listed the elements to be considered in a foodborne risk profile and the types of information required as: (i) description of an AMR food safety issue (AMR hazard of concern, antimicrobial agent to which resistance is expressed, food commodity with which AMR is associated); (ii) information on the AMR microorganism(s) and/or determinant(s) (source, transmission route, pathogenicity, virulence, linkage to resistance, growth and survivability, distribution, frequency and concentration in food chain, inactivation in foods (pH, D-value), characteristics of resistance (mechanism, location, cross-resistance, co-resistance, transferability between microorganisms)); (iii) information on the antimicrobial agent(s) to which resistance is expressed – non-human use (class; non-human uses; formulation; distribution; cost and availability; purpose – feed, food animals, food processing, sector; routes of administration – individual, mass medication, systemic; frequency; potential for extra-label use; potential role of cross- and co-resistance on food production; trends in use; trends in relation between use and occurrence of AMR; spectrum of activity; indications of treatment; is it in the critically important antimicrobial list?; distribution; cost, availability; availability of alternative agents; trends in use in humans; information on emerging diseases due to microorganisms resistant to the antimicrobial agent or its class); (iv) information on food commodities (source – domestic or imported; volume of production; frequency and per capita consumption; description of food production to consumption continuum – primary production, processing, storage, handling, distribution and consumption; characteristics of food that may impact risk management; (v) information on adverse public health effects (characteristics of the disease caused by the AMR microorganism, trends in foodborne disease, frequency, severity, hospitalization rate and long-term complications, susceptible population, risk factors, epidemiological patterns, regional, seasonal, ethnic differences, consequences of AMR on disease outcome, loss of treatment options, increased frequency, severity of infection, prolonged duration, hospitalization requirement, mortality); (vi) risk management information (identification of management options to reduce AMR hazard in food production to consumption continuum, measures to reduce the risk of selection and dissemination of AMR, measures to minimize contamination, cross-contamination with AMR microorganism, effectiveness of current management practices based on surveillance or other data); and (vii) evaluation of available information and major knowledge gaps (uncertainty in available information, identification of knowledge gaps that could hamper risk management, including, if warranted, the conduct of risk assessment). Should risk profiling determine that a full RA is required, he then listed the next steps in the RA process as being: (i) ranking of food safety issues and setting priorities for risk assessment and management; (ii) establishment of preliminary risk management goals; (iii) establishment of risk assessment policy; and (iv) commissioning of the risk assessment. Dr Karunasagar then provided details of the various steps in the risk assessment process: hazard identification, hazard characterization, exposure assessment, risk characterization, and risk management options. In closing, he listed the latter as: (i) options for animal production (restricting extra-/off-label use, major label restriction, withdrawing of market authorization, developing and implementing national treatment guidelines targeting specific AMR food safety issues, promoting the use of rapid diagnostic tests and implementing biosecurity; (ii) options for animal feed (implementing programmes to minimize use of feed or ingredients that could be a source of AMR); (iii) options for dealing with animal and human wastes (designing procedures to control AMR in biosolids, waste water, manure and irrigation water); and (iv) options for postharvest measures (reprocessing, recall procedures).

3.4 Possible exposure pathways

(Dr Peter Smith, FAO Expert, Ireland)

16. Dr Smith spoke briefly on the three possible exposure pathways for aquaculture systems. The first pathway is the direct transfer of a resistant bacterium, the resistant zoonotic bacterium moving from an aquaculture facility to a human population. To accomplish this, a resistant bacterium must have been enriched by AMU in aquaculture, must transfer to and be capable of infecting humans, and infection of humans must require antimicrobial therapy. The second pathway is indirect, and involves the movement of a resistant non-zoonotic bacterium from an aquaculture facility to a human population. To complete this pathway, the bacterium possessing a resistance determinant must have been enriched by AMU in aquaculture, it must be capable of surviving in the human intestine, capable of transferring its resistant determinant to a human pathogen within the human intestine, and it must be cause an infection requiring antimicrobial therapy. The third pathway is also indirect, and involves the movement of a resistant determinant from an aquaculture facility to a human population. The resistance determinant must have been enriched by AMU in aquaculture. To complete this pathway, the resistance determinant must persist in the environment, in the environment it must transfer to a human pathogen, and the resistant human pathogen must be the cause of an infection requiring antimicrobial therapy.

3.5 Observations on the OIE RA framework and Codex framework

(Dr J. Richard Arthur, FAO Expert, Canada)

17. Dr Arthur began his presentation by stating that his perspective on RA comes from his practical experiences in import risk analysis (IRA); the need for practical, inexpensive, relatively rapid processes that can be adapted to developing-country situations and understood and managed by non-specialists (i.e. qualitative risk assessment methods); and an interest in developing the aquatics part of the OIE Code (OIE, 2018) that deals with RA for AMR (Chapter 6.5). After providing some very basic information on RA (What is risk? What questions does an RA attempt to answer?) and presenting the OIE and CAC RA frameworks, Dr Arthur then looked at the various approaches to determining what constitutes an acceptable level of risk (ALOR) and the approaches to hazard identification. Drawing from experiences in pathogen risk analysis (PRA) that might be applicable to AMR RA, he then presented a stepwise simplified process for a hypothetical qualitative PRA. For a PRA, he noted the following key points: (i) risk assessment is done individually for each hazard; (ii) if likelihood of entry is negligible, the assessment stops, while if it is non-negligible, we proceed to exposure assessment; (iii) if the likelihood of exposure is negligible, the assessment stops, while if it is non-negligible, we proceed to consequence assessment; (iv) if the consequence is negligible, the assessment stops, while if it is non-negligible, we proceed to risk estimation; (v) risk estimation gives us an estimate of the total risk posed by the hazard; (vi) preparing scenario trees and pathways helps to clarify thinking and to estimate entry and exposure likelihoods; they are also useful for consequence assessment and in communicating the process and results of RA to stakeholders. He then made some preliminary comparisons between the information given for AMR RA in Chapter 6.5 of the OIE *Aquatic Animal Health Code* (OIE, 2018) and CAC guidelines CAC/GL 77-2011 (CAC, 2011). He noted that Chapter 6.5 of the Code provides only a recommended outline of the RA process (which as per IRA, allows flexibility), and deals with both AMR risks to live aquatic animals and also foodborne AMR risks associated with their products (referring to CAC), while CAC deals only with risks to human health due to foodborne AMR. Chapter 6.5 does not provide detailed guidance on how to conduct an AMR RA, and other directly supporting documents have yet to be developed by the OIE. In contrast, CAC/GL 77-2011 (CAC, 2011) provides detailed guidance, and there are many other WHO documents providing additional support. There are apparently no completed RAs for AMR in cultured aquatic animals, while completed RAs exist for human AMR, as well as for terrestrial animals (pigs, cattle, poultry and perhaps others). Preliminary findings include: (i) there are many articles demonstrating AMR, providing guidance, urging action to manage AMR, conducting surveys, etc., however, few actual AMR risk assessments have been done; (ii) in general, AMR risk assessments seem to favour a quantitative approach (no qualitative risk assessments were found); (iii) unlike for IRA, AMR risk assessment as outlined by OIE and CAC does not seem to be a methodology that is routinely used by governments; and (iv) OIE supporting guidance for qualitative and quantitative risk assessment for AMR in

aquaculture systems is needed, as was done for IRA. In closing, Dr Arthur posed the following questions related to the use of RA methods for evaluating the risk of AMR in aquaculture systems: (i) What are the criteria to be used to identify a hazard? (How to separate potential hazards from possible hazards?); (ii) How to determine if a potential hazard poses a significant risk? (Can the appropriate level of protection/ ALOR concept be applied, or must the level of risk that is significant be defined for each AMR RA?); (iii) Can scenario trees and pathways analysis be used for aquatic AMR RA? (iv) Is RA a useful approach for reducing AMR in aquaculture systems, or can AMR be directly addressed by surveillance and monitoring programmes combined with hazard analysis and critical control point, better management practices, and/or good aquaculture practices?

3.6 Oral delivery of medicines through aqua feed: AMR risk factors

(Dr Carlos Zarza, Skretting Aquaculture Research Centre, Norway)

18. Dr Carlos Zarza began his presentation by discussing medicated feeds, which are also known as medicated aqua feeds, medicated feedstuffs and pharmafeeds. He noted that this is the preferred method for the delivery of veterinary medicines with prescription, antibiotics, antiparasitics and vaccines for aquaculture. Medicated feeds are produced by dedicated production lines in fish feed factories using top-coating and vacuum-coating technologies. In top-coating, a medicine premix is mixed first with the carrier feed in an industrial or pharmaceutical mixer with the help of a binding agent, generally fish or vegetable oil, while in vacuum-coating, the medicine premix is mixed first with the oil, and the mixture is then coated onto the carrier feed with the help of a vacuum process. He then listed the main antibiotics used in medicated feeds, the “critically important” being the quinolones (flumequine, enrofloxacin, oxolinic acid) and the macrolids (erythromycin, tylosine), while the “highly important” include the amphenicols (florfenicol), the sulfonamides and the tetracyclines (oxytetracycline, doxycycline). He then mentioned the main drivers for AMU as being, for salmon, salmonid rickettsial septicaemia (*Piscirickettsia salmonis*), bacterial kidney disease and enteric red mouth disease (ERM), while those for rainbow trout are RTFS, ERM, and Gram-positives. For seabass and sea bream, they are the Gram-negatives (*Vibrio*, *Photobacterium*, *Aeromonas*), while for other marine species, they are the Gram-positives (*Streptococcus*) and *Tenacibaculum maritimum*. Other important factors leading to the use of antibacterials include infections by intracellular and Gram-positive bacteria, skin syndromes of unknown origin, a “prophylactic” treatment approach, deficient health management practices, poor or high-risk environmental conditions, stress and immunodepression and vaccination failure. Dr Zarza then reviewed in detail the factors that can lead to an increased risk of AMR when treating fish populations with medicated feeds. These include: (i) farm health status (disease prevention and minimization of risk of infection and treatment, quick and accurate diagnosis, and avoidance of prophylactic treatment); (ii) medicine and premix (preventing misuse, overuse and underuse of antibiotics, and avoiding the use of critically important antibiotics); (iii) manufacturing of medicated feed (ensuring quality and the recovery and homogeneity of medicine; avoiding loss during transport and delivery to fish); and (iv) farm treatment (ensuring an adequate feeding regime and medicine exposure, and avoiding medicine loss in environment). He then listed the some best practices/recommendations for the oral delivery of medicated feeds as including: effective health management plans (including vaccination); avoiding prophylactic AMU and always ensuring proper diagnostics; surveillance of isolates, including susceptibility monitoring; avoiding the use of critically important antibiotics; careful calculation of medicine and premix dosage; quality control after manufacturing (avoiding cross-contamination and leaching); effective administration, including duration, number of meals and distribution; and appropriate training of personnel involved in manufacturing and delivery. Following a brief review of the *WHO Guidelines on the Use of Medically Important Antimicrobials in Food-producing Animals* (WHO, 2017), Dr Zarza outlined Nutreco’s commitment to four areas for regulatory action: (i) setting ambitious antibiotic reduction targets in food production without back doors; (ii) creating transparency by improving the monitoring of AMU; (iii) innovation focus to alternatives strategies; and (iv) adapting the regulatory framework so that nutritional health and performance attributes can be claimed. He then concluded by reviewing the use

involves collaborative work by the private sector and government to reduce AMU across the Chilean salmon industry.

3.7 The major diseases and control measures in Chinese mariculture

(Dr Wang Yin-geng, Yellow Sea Fisheries Research Institute (YSFRI), People's Republic of China)

19. Dr Wang first presented some information on Chinese aquaculture, remarking that China is the world's largest producer, contributing >60 percent of global aquaculture by volume. In 2017, more than 50 marine species were being cultured, producing some 20 million tonnes of product. Several major types of production systems are being used in the farming of marine species: indoor factory and recirculating systems, cage culture, pond culture and sea ranching. He then went on to present the major diseases affecting Chinese mariculture. These include acute hepatopancreatic necrosis disease (AHPND) in shrimp, caused by *Vibrio parahaemolyticus* (pathogenic or non-pathogenic strains), *V. harveyi*, *V. alginolyticus* and *V. campbellii*, with outbreaks occurring from 2008–2009 in Hainan, Guangdong and Guangxi provinces, in 2009–2010 in Tianjin, Hebei province, and from 2012–2013 in Shandong, Liaoning Province. The trend has thus been from south to north around China. The disease has a strong pathogenicity, is wide spread and causes high mortality. Only 5–7 days occur from the appearance of the early clinical signs to the onset of mass mortalities. In China, the economic losses to shrimp farming have reached to RMB 25 billion each year. AHPND had been found frequently in China's coastal areas, with prevalence as high as 80 percent, and in some areas, some strains are extremely drug resistant. Treatment methods vary between regions. The virulence gene VP^{pir} can transfer to other strains. The scientific questions raised are: Why has AHPND been epizootic for so long, more than 20 years? What causes the pathogenic bacteria to spread widely? What is the truth about the diversity of AHPND? and What are the pathogenic mechanisms of these bacteria? The technical questions include: Why is AHPND difficult to treat? (according to histopathology, the necrosis of the hepatopancreas and degeneration of mucosal tissues block digestion and absorption, while according to etiology, pathogen diversity makes treatment difficult). Other diseases important in Chinese mariculture include: white spot syndrome and bacterial white spot syndrome of shrimp; skin ulcer disease of finfish (caused by *Vibrio anguillarum*, *V. harveyi*, *V. fluvialis* and *V. splendidus*); ascites disease and enteritis of finfish (caused by *Vibrio carchariae*, *V. alginolyticus*, *V. harveyi* and *Edwardsiella tarda*); and sea cucumber bacterial ulceration syndrome, caused by *Vibrio splendidus* and *Pseudoalteromonas nigrifaciens* (this is the most important disease in sea cucumber cultivation, with mortalities of up to 90 percent and disease outbreaks usually occurring from January–April, when water temperature is under 8°C). Based on the studies, the following are considered the important bacterial pathogens in Chinese mariculture: *V. parahaemolyticus*, *V. harveyi*, *V. anguillarum*, *V. splendidus*, *V. fluvialis*, *V. alginolyticus*, *V. carchariae*, *Photobacterium damsela*, *E. tarda* and *P. nigrifaciens*. China uses an integrated approach to disease control that includes: (i) good disinfection (using “Tangning” (C₇H₁₆N₃Cl)_n, PHMG, which is safe for the environment and aquatic animals and considered better than iodine or chlorine); (ii) stocking healthy larvae via selective breeding for specific pathogen free and specific pathogen resistant postlarvae (PL); selecting healthy PL by molecular testing in order to screen out the individuals that will bring harmful pathogens into the system, and screening out weak PL; (iii) good water quality management (including application of probiotics); (iv) preventing the entry of pathogens by cutting off routes of infection; (v) early diagnosis of disease; (vi) applying effective drugs (using antibiotic susceptibility tests to determine the proper dosage and duration), using algae as a binder, rather than water or oil, being waterproof to avoid leakage of drugs; (vii) using polyculture (consumption of moribund individuals and reduction in numbers of harmful bacteria); (viii) using herbal medicines, which leave no residues, have no AMR risk occurrence associated with human beings, provide more choice to deal with any pathogens (not only bacteria, but also viruses and parasites) and are cheaper than other drugs.

3.8 The preliminary investigation on AMR of common pathogenic bacteria in freshwater culture

(Dr Jiang Lan, Pearl River Fisheries Research Institute (PRFRI), People's Republic of China)

20. Dr Jiang first discussed disease control in aquaculture, noting that bacterial pathogens have a high adaptability to environmental changes and typically show a preference for certain species and certain organs. Disease control includes medical, ecological and immunological control, and can involve the use of antimicrobial agents, antiparasitic agents, disinfectants and Chinese herbal medicines. He reported that nine antimicrobial agents are permitted for use in China: doxycycline, neomycin, thiamphenicol, florfenicol, enrofloxacin, sulfamonomethoxine, sulfanilamide/TMP, sulfamethazine/TMP and sulfamethoxazole/TMP. In the laboratory of PRFRI, a surveillance programme on AMR from diseased aquatic animals was begun in 1995, a surveillance programme on AMR in aquaculture in 2012, and a surveillance programme on AMR from aquatic animal origin in 2017. PRFRI uses the dilution method for susceptibility testing according to the Clinical & Laboratory Standards Institute (CLSI) and microbiological automatic instruments (the Vitek Compact 60 BD and the Phoenix™ M50 System). From 1995–2012, the resistance level of 21 antimicrobial agents to clinical *Aeromonas* isolates was determined and some resistance genes were identified. During 2012 to 2015, PRFRI launched an AMR investigation of *Aeromonas* from healthy fish and the environment in Guangdong Province that was supported by a project of the Special Fund for Agro-scientific Research in the Public Interest (2012–2016). The resistance level of 14 antimicrobial agents to *Aeromonas* isolated from fish and the environment during 2012 to 2015 was determined. The predominant species isolated from healthy fish and their breeding environment was *Aeromonas veronii* (56.4 percent, 522/925). Isolates from fish and the culture environment within the same integrated fish farm exhibited similar or identical genotyping patterns between the two molecular typing methods used. Dr Jiang finished his presentation by showing some results of studies on the integron-mediated resistance mechanism and on quinolone resistance in tilapia.

3.9 Drug-resistance research on pathogenic bacteria of mariculture in YSFRI

(Dr Zhang Zheng, YSFRI, People's Republic of China)

21. Dr Zhang began his presentation by giving some background information on the YSFRI, which is affiliated with the Chinese Academy of Fishery Sciences of the Ministry of Agriculture and Rural Affairs. Founded in 1947, the YSFRI is the most famous and comprehensive mariculture research institute in China. Since 2001, the YSFRI has conducted epidemiological research on marine fish, shrimp and sea cucumber. Most of this work has been focused on the northern coastline of China. However, in recent years, many diseased marine animal samples have also been collected from southern China. Many different marine animal species are cultured along China's northern and southern coastlines. Although about 70 percent of the diseases affecting them are caused by bacteria, the number of bacterial species is few, the most common being members of the genera *Vibrio*, *Edwardsiella*, *Photobacterium* and *Pseudoalteromonas*. Often, one pathogen can cause different diseases. After many years of work, YSRFI has constructed a large marine pathogenic bacteria bank containing more than 11 000 bacterial strains representing over 160 species. These strains were isolated from over 4 300 samples of diseased marine animals. A lot of work on AMR has been done based on material contained in this bacterial bank. For almost all strains, the morphology of colonies grown on trypticase soy broth, thiosulfate citrate bile salts sucrose agar and 2216E medium plates has been recorded. For detection of antibody resistance, a basic drug resistance test was carried out for each strain by the slip method, with a total 36 types of antibiotic being used. In order to ensure the consistency of experimental results, YSFRI has insisted on purchasing the drug slip from the same supplier throughout the past 18 years. For some important bacterial pathogens, we use the red tetrazoline (TTC) method to detect the minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC). The stock solution of antibiotic is successively diluted into eight concentrations by the two-fold gradient dilution method in a 96-well plate. The sample volume is 200 µL per hole, and includes 20 µL of antibiotic solution, 180 µL of bacterial suspension and 10 µL TTC as indicator. Continuous culture, cryopreservation (at -86 °C) and freeze-drying are the three main methods used to preserve bacterial strains in most laboratories. However, these methods can impact the AMR of bacteria. For *V.*

anguillarum, for example, its drug resistance was changed under different treatments. In continuous culture, the susceptibility to rifampicin, erythrocin, furaxone, gentamicin, doxycycline and compound sulfamethoxazole decreased, while in freeze-drying, the susceptibility to erythrocin, furaxone, gentamicin and compound sulfamethoxazole increased, and with cryopreservation, the susceptibility on sulfamethoxazole decreased. Thus different preservation methods can impact the MIC and MBC of different antibiotics for the same bacterial strain, but this effect is limited and irregular. The mechanism of AMR in *P. damselae* subsp. *damselae* based on complete genome analysis was recently carried out in YSFRI's laboratory. The genome consists of two chromosomes and two plasmids, totaling 4 252 294 bp with 3 751 coding sequences, 196 tRNA genes and 47 rRNA genes. Only one AMR gene (*bacA*) was detected in this strain, which correlated with resistance to bacitracin. The antibiotic resistance phenotype further indicated that this strain was resistant to 15 drugs, including penicillin, ceftazidime, pipemidic acid, streptomycin, cefalexin, cefoperazone, clarithromycin, acetylspiramycin, clarithromycin, amikacin, gentamicin, kanamycin, oxacillin, ampicillin and sulfamethoxazole. Collectively, the strain was resistant to about 41.6 percent of the tested drugs, indicating its strong resistance to antibiotics. This strain, as a special case, was resistant to a wide range of antibiotics, including β -lactams, cephalosporins, quinolones, aminoglycosides, macrolides and sulfonamides. However, according to our investigation, the net-cage farming area around Daqin Island has hardly used any antibiotics during the past 20 years. Therefore, it remains largely unknown why the strain showed strong antibiotic resistance in this environment. However, other studies have confirmed the dissemination of drug resistance genes among bacteria in the aquaculture environment. It is Dr Zhang's opinion that AMR is not directly determined by genotype or drug use and may be a very complicated process which needs our in-depth study. Based on our long-term research finding, the phenotypic characteristic of AMR can change under environmental stress, and this is an area that is worthy of further attention. In closing, Dr Zhang noted that since 2002 most antibiotics have been forbidden for use in Chinese aquaculture. The current focus is on the use of environmentally friendly disinfectants such as hydrogen peroxide (H_2O_2), povidone iodine ($C_6H_9I_2NO$) and macromolecule guanidine. Chinese herbs and probiotics are also the best choices to defend against diseases in marine fish farming. Some bacterial vaccines has been researched and used for flatfish on a pilot-scale in our laboratory, but more work is needed to obtain commercial application certification.

4. SESSION 2: WORKING GROUP TASKS

22. Following lengthy plenary discussions and a restructuring of the meeting programme and goals (see Section 6), the experts, as a starting point to RA, decided to develop Risk Profiles for two bacterial pathogens. They then considered the importance of four bacterial pathogen groups with regard to fish health and public health: *Vibrio* spp., *Aeromonas* spp., *Streptococcus* spp. and *Edwardsiella* spp., selecting *V. parahaemolyticus* and *Streptococcus* spp. for further consideration.

23. For Risk Profiling, the participants were then divided into two Working Groups as follows:

- Working Group 1: *V. parahaemolyticus*: Peter Smith, Carlos Zarza, David Verner-Jeffreys, Richard Arthur, Wang Yin-geng and Jiang Lan.
- Working Group 2: *Streptococcus* spp.: Iddya Karunasagar, Patricia Gaunt, Ólafur Valsson, Rohana Subasinghe, Zhang Zheng and Melba Reantaso.

24. In addition to developing a Risk Profile for their respective pathogens, each Working Group was asked to provide:

- A preliminary level of risk estimation reached based on the above risk profiling
- General comments on the usefulness/applicability (fitness for purpose) of the CAC risk profiling elements and process
- General recommendations for the risk assessment for *Streptococcus* spp. and *V. parahaemolyticus*

- General recommendations/considerations for improving the risk profiling and the general RA process for a better understanding of AMR in aquaculture (animal and human health)
- Other thoughts/recommendations with respect to integrated surveillance of AMU and AMR

25. An example of the results of Risk Profiling is presented in Annex 4, while the recommendations of the Working Groups have been integrated into Section 6. Conclusions and Way Forward.

5. SESSION 3: DISCUSSIONS ON POTENTIAL DEVELOPMENT OF A PROPOSAL TO CONTRIBUTE TO A MULTISECTORAL PROJECT

26. Session 3, chaired by Dr Rohana Subasinghe, was held on the afternoon of Day 3. This Session involved a plenary discussion on the potential development of a proposal to contribute to a multisectoral project, “Towards reducing aquaculture-based AMR through a cross-sectoral approach.”

27. There was consensus among the participants to explore potential future projects and activities and mobilize necessary resources. An FAO Regional Technical Cooperation Project (RTCP) on “Alternative ways to reduce the use of antimicrobials in aquaculture” can be developed. The project would have the People’s Republic of China and India as the main focus countries and would assess current practices, putting science into those practices and eventually transferring and further disseminating such technology, if proven appropriate and successful. The Fleming Fund could be approached for harmonization of antibiotic susceptibility testing methods, including capacity building to support integrated surveillance. The candidate FAO Reference Centers on AMR and Aquaculture Biosecurity can be tapped. A second follow-up meeting of the Expert Working Group should be organized, and the People’s Republic of China has already expressed interest to host this meeting.

6. CONCLUSIONS AND WAY FORWARD

28. Dr Melba Reantaso presented the Conclusions and Way Forward, noting that the information given represented a draft for discussion. She began by summarizing the original process, recalling that there was little information on RA for AMR. These include:

- a probabilistic risk assessment for eight different aquaculture production scenarios in Asia by Rico and Van den Brink (2013) made by combining up-to-date information on the use of veterinary medicines and aquaculture production characteristics;
- there might be some work done for the terrestrial sector; and
- some tools are being developed by the tripartite (WHO, OIE and FAO) for an integrated RA.

29. The original objective of the Expert Working Group Meeting was to attempt to prepare an AMR Risk Profile for a selected aquaculture system, and then, having completed this scoping exercise, to attempt to take a previously selected hazard for the selected aquaculture system through the major technical portions of the RA process (i.e. risk assessment; risk management, risk evaluation) as outlined in the OIE *Aquatic Animal Health Code, 2018* (OIE, 2018) and using a qualitative RA approach.

30. The experts tried to determine whether RA is a tool that has practical application for evaluating hazards associated with AMR in aquaculture, determining if an identified hazard poses a significant risk to aquaculture and/or human society, and if so:

- identify ways to reduce the level of risk to an acceptable level;
- look at the various steps in the RA process as outlined by the OIE Code (OIE, 2018) and CAC guidelines CAC/GL 77-2011 (CAC, 2011) to see if adequate information is available to allow calculation of a risk estimate, identify any areas of the RA process where difficulties are likely to occur, and suggest ways of dealing with these problem areas; and

- briefly look at the possibility of preparing a proposal for a multisectoral (aquaculture, livestock, human medicine) AMR RA, including a justification, approach, possible participants and potential funding agencies.

31. She then briefly outlined the actual process that was followed using the following table:

	Morning: 08:30; Coffee (10:30–11:00); Lunch (12:30–13:45)	Afternoon: Coffee (15:30–16:00); until 17:30	
Day 1 26/11/18	Session 1: Setting the scene: background with technical presentations Recent global and regional initiatives to reduce AMR What is AMR? Overview and current status of knowledge AMR RA for human medicine: the WHO framework and guidance AMR RA for aquaculture: OIE framework	Session 1: Setting the scene: background with technical presentations Observations on the OIE RA framework and CAC framework Oral delivery of medicines through aqua feed: AMR risk factors Plenary discussions on revising the agenda	
Day 2 27/11/18	Session 1: Setting the scene: background with technical presentations: the People’s Republic of China (3 presentations) Session 2: Risk Profiling: Plenary discussions on four bacterial pathogen groups: <i>Vibrio</i> spp., <i>Aeromonas</i> spp., <i>Streptococcus</i> spp., <i>Edwardsiella</i> spp. using agreed criteria (fish health and public health) Two Working Group tasks: Risk profiling	Group 1: <i>V. parahaemolyticus</i> Peter, Carlos, David, Richard, Wang, Jiang WG discussion and presentation	Group 2: <i>Streptococcus</i> spp. Karun, Patricia, Ólafur, Rohana, Zhang, Melba WG discussion and presentation
Day 3 28/11/18	Session 2: Continue risk profiling using CAC Risk Profile elements + below <ul style="list-style-type: none"> • Preliminary level of risk estimation reached based on above risk profiling • General comments on the usefulness/applicability (fitness for purpose) of the CAC risk profiling elements and process • General recommendations re: risk assessment for <i>Streptococcus</i> spp. and <i>V. parahaemolyticus</i> • General recommendations/considerations for improving the risk profiling and the general RA process for better understanding of AMR in aquaculture (animal and human health) • Other thoughts/recommendations with respect to integrated surveillance of AMU and AMR Session 3: Plenary discussions Discussions on potential development of a proposal to contribute to a multisectoral project “Towards reducing aquaculture-based AMR through a cross-sectoral approach”		
Day 4 29/11/18	Conclusions and the Way Forward Round table discussions on FAO Reference Centers on AMR and Aquaculture Biosecurity Free afternoon		

32. In closing, Dr Reantaso summarized the general observations and recommendations of the participants as follows:

On using RA as a decision-making tool for assessing the risk of AMR in aquaculture:

- The CAC guidance was useful in assisting with the risk profiling process, but it would be helpful to review and adapt as appropriate this guidance to profiling for aquatic AMR RA.
- Considering the limited guidance provided by the OIE Aquatic Code (OIE, 2018) for risk profiling on AMR in aquaculture, the Group decided to use the Codex guidelines (CAC, 2011), as an alternative. Although the Group did not examine the OIE guidelines on aquatic AMR, given the rapid development in diagnostic methods which will influence the understanding of the spread of aquatic AMR, the Group is of the opinion that it would be useful to examine the OIE aquatic AMR guidelines for continuing this work and the dialogue.
- More research are needed to address the question on whether there are strain differences with respect to host specificity and to address the use of antibiotics in host (aquatic animal) specificity.

On the risk profiling for Streptococcus spp. and V. parahaemolyticus

- Two of the four important bacterial pathogens (i.e. *Streptococcus* spp., *V. parahaemolyticus*) were selected for AMR risk profiling, and in both cases the risk profiling done by the Working Groups concluded that the AMR risks posed by these pathogens were likely to be low or very low due to the very low epidemiological link and absence of AMR-associated infections. It was thus concluded that conducting a full risk assessment was not recommended for any of the pathogens evaluated (*S. agalactiae*, *S. inae*, *Lactococcus garviae* and *V. parahaemolyticus*).
- For *V. parahaemolyticus*, there is no apparent eminent risk associated with consumption of fish on AMR development in public health.
- However, the Singapore outbreak of *S. agalactiae* indicates that the situation with regard to this species needs to be monitored. More data are needed on fish-associated *S. agalactiae* strains, their virulence, sero- and genotypes and antibiotic susceptibility properties.
- There was no evidence that the use of these drugs with other organisms is causing collateral damage (rise in AMR in *V. parahemolyticus*). It should be noted that the strains of *V. parahaemolyticus* diagnosed in shrimp are distinct from those causing problems in humans.

On recommendations with respect to integrated surveillance of AMU and AMR

- A harmonized international surveillance system should be established to determine the incidence of *S. agalactiae* in farming systems. This surveillance should be done using standardized protocols related to sampling (based on epidemiological data (i.e. prevalence, seasonality, etc.), and susceptibility testing based on ecological and clinical breakpoints would be needed. More information on antimicrobial use in different countries practicing aquaculture would be needed.

On recommendations for improving the risk profiling and the general RA process for better understanding of AMR in aquaculture (animal and human health)

- More data on prevalence, abundance in aquaculture farms and fish species in the primary production to fish consumption continuum is needed. The AMR situation in fish-associated strains of *V. parahaemolyticus* needs to be continuously monitored.
- Antibiotics are essential for the health and welfare of animals and are still required. When using antimicrobials, it is important to stress the prudent AMU.

- Consider redrafting the risk profiling chapter to capture the two main questions raised above. To take into consideration the United Nations Sustainable Development Goals: SDG 2 – Zero Hunger and SDG 3 – Good Health and Well-being.
- Animal health and welfare are important issues that greatly impact food security in animal food production. These issues should also be taken into consideration in their own right.

Specific recommendations for continuing the current work

- For risk reduction, more work on improved husbandry and rearing conditions should be done, only the quantity of feed that animals will consume should be given, and vaccines, biosecurity (animal husbandry) and animal welfare should be improved.
- Specific experts from the clinical and animal sectors working on *S. agalactiae* should be engaged. Collection of data on prevalence and abundance of *S. agalactiae* in aquaculture in different countries should be promoted, particularly those countries involved in the culture of tilapia and other susceptible species.

Other recommendations with respect to integrated surveillance of AMU and AMR

- *S. agalactiae* affects humans, bovines and fish, and in all these sectors. Antibiotics are used for treatment. Hence, integrated surveillance would prove very useful to understand the emergence and spread of resistance across and within sectors.
- EUCAST and CLSI: organisms that test at 35°C. EUCAST not testing at lower temperature (18, 22, 28°C); only CLSI. Epidemiological cutoff values.
- OIE document suggests when doing surveillance of AMR the raw data should be published and the data processed.

On the development of a programme for an integrated sectoral approach to reducing AMR, there was consensus to explore and mobilize resources for potential future projects and activities:

- Development of an FAO RTCP on “Alternative Ways to Reduce the Use of Antimicrobials in Aquaculture” can be explored. The project would have the People’s Republic of China and India as the main focus countries and would assess current practices, putting science into those practices and eventually transferring and further disseminating such technology, if proven appropriate and successful.
- The Fleming Fund and CLSI could be approached for harmonization of antibiotic susceptibility testing methods, including capacity building to support integrated surveillance.
- The candidate FAO Reference Centers on AMR and Aquaculture Biosecurity can be considered as collaborators and technical service providers.
- A second follow-up meeting should be organized (agenda to be developed); the People’s Republic of China has expressed interest to host this meeting.

Ideas submitted by proponents for potential future projects and activities:

From the People’s Republic of China:

- **Development and establishment of the “global aquaculture demonstration systems for reducing AMR”.** Through this programme, AMR could be reduced through application of risk-based, collaborative and progressive biosecurity management (i.e. via a Progressive Management Pathway for Aquaculture Biosecurity (PMP/AB)), healthy aquaculture technologies, and antibiotic alternatives/substitutes, etc. to develop environmentally friendly culture systems which could be promoted as demonstration systems worldwide.

- **“Establishment of a potential system on “Shrimp Farming with Zero Antibiotic Use”.** This programme will focus on developing standard operating procedures for shrimp culture with antibiotic substitutes and alternatives other than antibiotics.
- Funding sources include the Government of the People’s Republic of China and collaborating partners.

From Mississippi State University (MSU):

- **Further studies on atypical *Aeromonas hydrophila* from field outbreaks in the southeastern United States of America:** Isolation, biochemical and molecular characterization, sequencing, MIC and susceptibility testing and establishing critical cutoff values; efficacy of treatment with antibiotic-medicated feed.
- Funding source possibilities include the United States Agency for International Development Innovation Lab and the United States Department of Agriculture catfish health grant.

The next steps

33. Dr Reantaso then concluded her presentation by outlining the next steps to be taken as including:

- preparation of the Workshop Report, a narrative to capture the main discussion points and conclusions.;
- possibility of drafting a paper to be submitted to a journal on AMR Risk Profiling for *V. parahaemolyticus* and *Streptococcus* spp. (to be discussed); and
- planning for the next follow-up meeting.

7. CLOSING REMARKS

34. Dr Reantaso thanked and expressed appreciation to the experts for their keen participation and wished them a safe journey home.

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ANNEX 1

Draft annotated programme

Date	Activities
25 November (Sun)	<ul style="list-style-type: none"> • Arrival of working group members
26 November (Mon)	Day 1
08:30-09:00	<ul style="list-style-type: none"> • Welcome • Self-introduction of Expert Working Group Members • Introduction to the Expert Working Group Meeting agenda: the 4 Ps and adoption of agenda (M. Reantaso)
Annotation: If agenda is adopted by experts, the programme as outlined will proceed. If not, and changes are introduced, the schedule will be revised accordingly.	
09:00-10:30	Background presentations <ul style="list-style-type: none"> • Recent global and regional initiatives to reduce AMR (M. Reantaso) • What is AMR? Overview and current status of knowledge (D. Verner-Jeffreys) • AMR RA for human medicine: the WHO framework and guidance (I. Karunasagar) • AMR RA for aquaculture: the OIE framework (P. Smith) • Observations on the OIE RA framework and CAC framework (R. Arthur)
Annotation: The background presentations are aimed at putting everyone on the same page. If experts feel that there are other essential presentations needed, these will be considered.	
10:30-11:00	Coffee break and group photo
11:00-12:30	Presentation of major components for a draft case profile <ul style="list-style-type: none"> • The selected aquaculture system – state of knowledge (R. Subasinghe) • Hazard Identification: selection criteria, the selected hazard - status of knowledge (P. Smith and I. Karunasagar) • Group discussion of case profile
Annotation: Selection criteria might include such things as (i) identification of a food safety issue, detection of AMR in bacteria or determinants, knowledge that an antimicrobial is being misused in a particular aquaculture system (e.g., prophylactic use, improper dosage, etc.) For consideration: <ul style="list-style-type: none"> • “hazard” would be an aquatic bacterium that is a pathogen of a cultured species and an actual or potential pathogen of humans, that has developed AMR to an antibiotic that is important in human medicine, due to the use or misuse of this antibiotic by aquaculturists. • status of aquaculture development, human and livestock populations in the area likely to be impacted. 	
12:30-13:45	Lunch break
13:45-15:30	Working Groups (1 and 2) Session 1: Improving the case profile and defining the RA process <ul style="list-style-type: none"> • Working Group 1: Case profile • Working Group 2: RA process (methodology, definitions of risk levels, combining risk estimates, how to assess consequences, ALOR, dealing with uncertainty, etc.)

Annotation: Group 1 will consider whether any essential information is missing from the Risk Profile. Group 2 will review the RA process and make recommendations as to the procedures to be followed during the risk assessment. Both groups to draw upon CAC/GL 77-2011 for guidance.	
15:30-16:00	Coffee break
16:00-17:30	Working Group presentations, recommendations and discussion
27 November (Tues)	Day 2
08:30-10:30	Working Groups (3 and 4) Session 2: Risk Assessment: Estimation of Risk of Entry and Establishment <ul style="list-style-type: none"> Working Group 3: Entry and Establishment in Aquaculture Systems Working Group 4: Entry and Establishment in Human Populations
Annotation: Drawing upon the information presented in the Risk Profile, and using the methods selected by Group 2, and if possible, a pathways analysis approach, the Working Groups will attempt to arrive at an estimate of the respective risks of entry and establishment. The end product of this exercise should be a combined risk estimate for entry and establishment (R_{entry} and $R_{\text{establishment}}$).	
10:30-11:00	Coffee break
11:00-12:30	Working Groups Session 2 (Continued)
12:30-13:45	Lunch break
13:45-14:30	Presentation of Working Groups Session 2 Results <ul style="list-style-type: none"> Working Group 3: Results of estimation of risk of entry and establishment for aquaculture system Working Group 4: Results of estimation of risk of entry and establishment for human populations
14:30-15:30	Working Groups (5 and 6) Session 3: Risk Assessment; Consequence Assessment <ul style="list-style-type: none"> Group 5: Consequence assessment for aquaculture Group 6: Consequence assessment for human medicine
Annotation: Using the agreed upon definitions for levels of consequence and method for combining consequences, the Working Groups will identify likely consequences, attempt to estimate their level of significance, and combine these estimates into a single estimate of consequence for each sector.	
15:30-16:00	Coffee break
16:00-17:30	Working Groups Session 3 (continued)
28 November (Wed)	Day 3
08:30-10:30	Working Groups Session 3 (continued)
10:30-11:00	Coffee break
11:00-12:00	Presentation of results of Session 3: Consequence Assessment and (factors considered, estimate of consequence level, identification of missing information, recommendations) <ul style="list-style-type: none"> Working Group 5 (consequences to aquaculture) Working Group 6 (consequences to human society/medicine)
12:00-12:30	Plenary discussion: Risk Estimation <ul style="list-style-type: none"> aquaculture human medicine
Annotation: Using the risk estimates for entry, establishment and consequence, estimates of total risk will be calculated for (i) aquaculture and (ii) human medicine	
12:30-13:45	Lunch break
13:45-15:30	Plenary discussions on Risk Management <ul style="list-style-type: none"> Risk evaluation Risk management options

Annotation:	
<ul style="list-style-type: none"> • Using the previously agreed-upon ALOR, risk evaluation will determine if the total risk calculated for each sector is acceptable. • Assuming that an aquaculture system is using antimicrobials, what are the minimum risk management measures for reducing AMR risks that need to be in place? • Getting this far in the RA process will determine whether a RA is possible. Due to time constraints, we will not take the various risk management measures into the risk assessment process (option evaluation). • Recommendations for risk communication will be dealt with separately. 	
15:30-16:00	Coffee break
16:00-17:30	Discussions on potential development of a proposal to contribute to a multisectoral project “Towards reducing aquaculture-based AMR through a cross-sectoral approach” (R. Subasinghe)
29 November (Thurs)	Day 4
0830-10:30	Proposal development (continued)
10:30-11:00	Coffee break
11:00-12:30	Wrap up and way forward (M. Reantaso) <ul style="list-style-type: none"> • Review of meeting results • Recommendations to FAO and others Future Expert Working Group actions/activities (funds permitting)
12:30-13:45	Lunch break
Afternoon	Departure of some participants
30 November (Fri)	Departure of all remaining participants

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ANNEX 3

Group photographs



Figure 1. Group photo of the FAO Expert Group Meeting. First row (left to right): Dr P. Smith (Ireland), Dr P. Gaunt (USA, MSU), Dr M. Reantaso (FAO), Dr W. Yin-geng (China, YSFRI); Ms E. Irde (FAO); second row: Dr J. Lan (China, PRFRI), Dr B. Hao (FAO), Dr R. Subasinghe (Sri Lanka, Futurefish), Dr I. Karunasagar (India, Nitte University), Dr C. Zarza (Norway, Skretting), Dr R. Arthur (Canada), Dr D. Verner-Jeffreys (UK, Cefas), Dr Ó. Valsson (Botswana, OIE), Dr Z. Zheng (China, YSFRI).



Figure 2. Group photo of the FAO Reference Center on AMR and Aquaculture Biosecurity. Left to right: Dr Z. Zheng (China, YSFRI), Dr I. Karunasagar (India, Nitte University), Dr J. Lan (PR China, PRFRI), Dr P. Gaunt (USA, MSU), Dr M. Reantaso (FAO), Dr W. Yin-geng (China, YSFRI), Dr B. Hao (FAO).

ANNEX 4

Example working group risk profile:

AMR Risk profile matrix for *Streptococcus* spp.

	<i>Streptococcus agalactiae</i>	<i>Streptococcus iniae</i>	<i>Lactococcus garviae</i>
1. Description of the AMR food safety issue	So far, there is no evidence of an AMR food safety issue related to <i>S. agalactiae</i> . However, since there have been human cases associated with this organism and tilapia, which is an important aquaculture species, it was decided to go through the process for this organism. This organism affects a broad range of taxa including fish, humans, bovines and other mammals.	So far, there is no evidence of an AMR food safety issue related to <i>S. iniae</i> , but this organism was discussed due limited zoonotic potential, mainly through contact.	So far, there is no evidence of an AMR food safety issue related to <i>L. garviae</i> , but this organism was discussed due limited zoonotic potential.
2. Information on AMR microorganism(s) and/or determinant(s) Characteristics of the identified foodborne microorganism(s)	There are diverse strains associated with different species. Reports indicate that strains colonizing humans (female genital tract), bovines and fish could be distinct populations. Human clinical strains belong to serotypes Ia, II, III and V. Serotypes Ia and III are commonly haemolytic. Fish-associated infections were reported to be largely due to serotype Ib, although serotype III has been occasionally reported; infections caused by serotype II are rare. These are non-haemolytic strains (e.g. ST261). Bovine strains belong to different geno- and serotypes. Sequence type 103 belonging to serotype II was found in Nile tilapia in Brazil, and this serotype is common in bovines in Denmark and China.		

	<p>Although there have been speculations about transmission between bovine and fish species, there has been no confirmed epidemiological link. Although different strains have been associated with different species, some overlap could be seen in some cases. Clinical strains are resistant to tetracycline (over 80%). About 20% are resistant to erythromycin. There is very little information on resistance in fish-associated strains. There have been no reports of human infections with resistant strains from fish.</p>		
<p>3. Information on the antimicrobial agent(s) to which resistance is expressed. Class of the antimicrobial agent(s)</p>	<p>Clinical strains are resistant to tetracycline (over 80%). About 20% are resistant to erythromycin. There are reports of tetM in humans and tetO in bovine strains. Erythromycin resistance was due to ermB, ermTR, and mefA in clinical isolates and ermB in bovine strains. In clinical strains, TetM is carried on a conjugative transposon. There is experimental evidence that this transposon can be mobilized into <i>Enterococcus faecalis</i>. But in the case of fish-associated strains, the information is limited to reports in the Chinese literature of sulphonamide resistance in 86% of isolates. In China, florfenicol is used in tilapia. Herbal treatment and vaccine are also common. From other areas, there are limited reports of use of erythromycin and tetracycline.</p>		<p>Antibiotics have been used to treat fish. Lincomycin, oxytetracycline and macrolides (erythromycin, spiramycin, kitasamycin and jasomycin) have been used in Japan. In Europe, erythromycin, amoxicillin and doxycycline have been used. Emergence of resistance to antibiotics has been reported. Resistance determinants Tet (S) and ermB have been observed in R plasmids. Quinolone resistance due to mutations in gyrA and parC genes has been recorded.</p>

<p>4. Information on food commodity(ies)</p>	<p>The main aquaculture species affected by <i>S. agalactiae</i> is tilapia. A wide range of other species, both freshwater and marine can be affected These include barramundi, sting rays, snakehead, bighead carp, mullet, Pompano, <i>Schizothorax prenanti</i>, pike perch and <i>Scortum barcoo</i>. Tilapia is generally processed and cooked; however, some species may be eaten raw as a part of sushi or salads (as in Singapore). Reports of infection may be rare, since most of the fish are consumed after cooking. There could be a perceived risk for fish handlers, but there are no confirmed clinical reports related to this. In China, a study showed the presence of <i>S. agalactiae</i> in 60% of the fish from 10 fish farms.</p>	<p>Over two dozen fish species are affected, including Japanese flounder, tilapia, coho salmon, rainbow trout, yellowtail, <i>Selenotoca multifasciata</i>, yellow catfish (<i>Pelteobagrus fulvidraco</i>) red drum, <i>Trachinotus ovatus</i>, sea bass (<i>Lateolabrax japonicas</i>, <i>Lates calcarifer</i>), and yellowfin seabream (<i>Sparus latus</i>).</p>	<p>Affects a wide variety of fish including Japanese eel, Red Sea wrasse, Nile tilapia, olive flounder, amberjack, king fish (<i>Seriola quinqueradiata</i>), rainbow trout, grey mullet, catfish (<i>Silurus glanis</i>), <i>Paralichthys olivaceus</i>, <i>Trachinotus ovatus</i>, <i>Larimichthys crocea</i>, freshwater prawn, bottlenose dolphin, octopus and freshwater turtle.</p>
<p>5. Information on adverse public health effects</p>	<p>There are no reports related to AMR infection related to food. Most of the human cases are neonatal infections due to infection acquired during birth through exposure to commensal strains (typically carried by 10–20% of the population) in the birth canal. There are occasional reports of food-borne and other infection routes. Mostly these are associated with immunocompromised/elderly individuals. However, a recent fish-borne outbreak in Singapore was perhaps due to a highly virulent strain belonging to sequence type 238. This strain seemed to affect even healthy individuals; the number of cases reduced dramatically after controls were put in place.</p>	<p>There are no reports of AMR infection related to food. There are very limited cases associated with immuno-compromised individuals, mainly through contact. Considering the extent to which affected fish are consumed internationally, the epidemiological link is very low.</p>	<p>There are no reports related to AMR infection related to food. There are very limited cases associated with immuno-compromised individuals. Considering the extent to which affected fish are consumed internationally, the epidemiological link is very low.</p>

6. Risk management information	For fish health and associated reduction in carriage and infection, good biosecurity including restriction of movements of live fish would be important. Commercial vaccine is available, but possibly not able to respond to changing pathogen populations (genoserotype) quickly enough. Nevertheless, vaccination should be considered as an important risk management measure. For human infections, cooking would be a good management measure. In Singapore, where consumption of raw fish is common, the outbreak led to advice to cook fish before consumption.	Vaccines are available for grouper and tilapia (bivalent vaccine for <i>S. iniae</i> and <i>S. agalactiae</i>).	Vaccination has been recommended to protect the fish against lactococcosis. Commercial vaccines are available.
7. Evaluation of available information and major knowledge gaps	There is limited information of carriage in healthy fish, and limited data on AMR in fish-associated strains. More genotypic and phenotypic information on fish-associated strains is needed.		
8. Preliminary level of risk estimation reached based on the above risk profiling	With AMR <i>S. agalactiae</i> , there is very limited information on fish-associated human infections. Most fish-associated strains have very low zoonotic potential. Further, tilapia is a highly consumed fish globally and the epidemiological link is very low. However, recent fish-associated human infections in Singapore raise some concerns.	Given the lack of epidemiological link between fish consumption and human infection, the level of risk to public health is very low.	Given the lack of epidemiological link between fish consumption and human infection, the level of risk to public health is very low.

An FAO Expert Working Group Meeting “Scoping exercise to increase the understanding of risks of antimicrobial resistance (AMR) in aquaculture” was held at the Mondello Palace Hotel, Palermo, Italy from 26–29 November 2018.

A risk profiling exercise was conducted on two bacterial agents important to both animal and human health, namely: *Streptococcus* spp. and *Vibrio parahaemolyticus*. These bacterial agents affect tilapia and shrimp, respectively, top aquaculture species that contribute significantly to global food and nutrition security. The risk profiling exercise for the two bacterial pathogens revealed that, in both cases, the AMR risks posed by these pathogens were likely to be low. Strain differentiation and pathogenicity as outlined in Codex Alimentarius are essential in understanding the AMR risks posed by bacteria affecting aquaculture production.

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