Status of Viet Nam's National Action Plan on Antimicrobial Resistance in Aquaculture

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Abstract

Antibiotic resistance has been considered as one of the biggest global concerns in terms of negative impacts on public health, resistant pathogens and environmental problems. This paper aims to review the present status in Viet Nam regarding Antibiotic Use (AMU) and Antibiotic Resistance (AMR) in aquaculture. To implement the National Action Plan (NAP) on Drug Resistance 2013–2020, the Vietnamese Government has established a national public health network that follows the "One Health Approach" and the National Steering Committee for Prevention and Control of Aquatic Animal Diseases, AMU and AMR in Aquaculture. The Government has also issued the NAP for Controlling AMU and AMR in Livestock Production and Aquaculture period 2017–2020. To promote awareness, national television programs and communication campaigns were conducted to increase awareness of AMR among farmers and other stakeholders. Farmers were also instructed on proper AMU and provided vital information on AMR. Pilot projects on the surveillance for AMR in cultured catfish and the use of antibiotics in shrimp and catfish aquaculture were carried out to gather evidence on AMU and AMR status in the country. In addition, households raising tilapia and traditional freshwater fish were interviewed for information on AMU and AMR in freshwater fish aquaculture. To promote best practices, programmes for aquatic animal disease control were established and trainings on good antibiotic use in aquaculture carried out. Best practices in the culture of shrimp, catfish, tilapia and other species have also been improved through the use of programmes such as VietGAP and GlobalGAP.

Keywords: survey, shrimp, catfish, traditional freshwater fish, *Aeromonas*, *Streptococcus*

Introduction

Antimicrobial resistance (AMR) is considered as one of the greatest threats to public health worldwide. At the international level, the Food and Agriculture Organization of the United Nations (FAO), the World Organization for Animal Health (OIE), and the World Health Organization (WHO) collaborating through a Tripartite Agreement have identified AMR as one of the three priority topics for joint actions (FAO/OIE/WHO, 2011) and have developed a Global Action Plan on Antimicrobial Resistance (WHO, 2015). Following a "One Health Approach", the Global Action Plan provides a framework for national action plans (NAPs) to combat AMR.

In Viet Nam, the Ministry of Health (MoH) has initiated national activities to tackle AMR with the publication of the National Action Plan on Combatting Drug Resistance from 2013 to 2020 (MoH, 2013). The overall objective of the plan is to promote the prevention of drug resistance, contributing to improving the quality and effectiveness of the prevention and control of epidemics, medical examinations and treatments to protect, care for, and improve people's health. It includes six specific objectives, one of which is the promotion of proper antimicrobial use in livestock, poultry, aquaculture, and cultivation.

Because of the rapid expansion in the aquaculture area and the use of increased stocking densities, Vietnamese aquaculture has been faced with serious disease outbreaks. Major diseases and pathogens of concern include white spot disease (WSD) and acute

hepatopancreatic necrosis disease (AHPND) in shrimp; *Edwardsiella ictaluri* and *Aeromonas hydrophila* infections in catfish *Pangasianodon hypophthalmus* (Sauvage, 1878); *Streptococcus* spp. and *A. hydrophila* infections in tilapia *Oreochromis niloticus* (Linnaeus, 1758); and *Aeromonas* spp. and *Pseudomonas* spp. infections in "traditional freshwater fish" such as common carp *Cyprinus carpio* Linnaeus, 1758, grass carp *Ctenopharyngodon idella* (Valenciennes, 1844), silver carp *Hypophthalmichthys molitrix* (Valenciennes, 1844), climbing perch *Anabas testudineus* (Bloch, 1792). As a result, antimicrobials play a critical role in the prevention and treatment of aquatic animal diseases. However, their imprudent use and overuse have been contributing factors in the spread of antimicrobial resistance (AMR). In this paper, we detail the status of the aquaculture component on the Vietnamese National Action Plan for AMR, in reference to the four pillars of the FAO Action Plan on AMR (FAO, 2016): i.e. governance, awareness, evidence or surveillance, and best practice.

Implementation of AMR Action Plan

Viet Nam is the first country in the World Health Organization's (WHO) Western Pacific Region that has approved a NAP on combating antibiotic resistance. Viet Nam has also established a national public health network to implement the "National Action Plan on Drug Resistance 2013–2020", according to Decision No. 2174/QD-BYT dated 21/6/2013 in which the Ministry of Health (MOH) is the lead agency and the Ministry of Agriculture and Rural Development (MARD) is one of the key implementing agencies (MoH, 2013). The main objective of the NAP is to improve people's health care through preventing and controlling drug resistance and raising the quality and effectiveness of medical examination. The NAP consists of six main activities: (1) raising awareness of community and health staff about drug resistance; (2) strengthening and improving the capacity of the national surveillance system on AMU and AMR; (3) ensuring a supply of essential drugs of high quality; (4) promoting the safe, prudent and responsible use of drugs; (5) strengthening the control of infections; and (6) strengthening the prudent and responsible use of antibiotics in agriculture, livestock production, and aquaculture.

In order to further support this multisectoral approach to the control of AMR, in October 2016, the MoH established the National Steering Committee on Prevention of Antimicrobial Resistance for the period 2016–2020 (Decision 5888/QD-BYT dated 10/10/2016). The committee included 31 members from four ministries, as well as members of external partner institutions. AMR was identified as a key component of the Global Health Security Agenda of Viet Nam through which is a five-year plan to prevent and control the emergence and spread of AMR through the effective and rational use of antibiotics in humans and animals was also established. By May 2018, several activities were conducted or were undertaken. These include: (1) organising an annual communication activity/meeting on AMU and AMR in November, since 2013; (2) developing regulations and technical guidelines on clinical pharmacological activity, drug use in treatment, and drug description; (3) preparing standardised professional materials and protocols related to disease diagnosis and treatment with antibiotics; (4) implementing an Aide Memoire on Multi-stakeholder Engagement to Combat AMR in Viet Nam (led by the Department of Animal Health (DAH) of MARD and the Drug Administration of Viet Nam of MoH) (MoH/MARD/MOIT/MONRE, 2015); (5) increasing awareness of AMU and the risks of AMR; and (6) issuing, by MARD, of Decision No. 2625/QD-BNN-TY dated 21/6/2017 on "National Action Plan (NAP) for Controlling Antimicrobial Use and Antimicrobial Resistance in Livestock Production and Aquaculture (2017–2020)" (Decision No. 2625/QD-BNN-TY dated 21/6/2017)(MARD, 2017a).

The main objective of this NAP is to mitigate the risk of antibiotic resistance in public health through controlling antibiotic use in livestock production and aquaculture (MARD, 2017a). Major activities of the NAP include (1) strengthening and consolidating the state management of AMU and AMR; (2) improving the legal basis for AMU and AMR management; (3) enforcing the regulations and technical guidelines currently in place; (4) increasing awareness of AMU and the risks of AMR; (5) implementing good treatment and husbandry practices in livestock feed manufacturing and livestock production and aquaculture; (6) monitoring AMU, AMR and antibiotic residues; and (7) strengthening inter-sectoral collaboration in AMR management. Under this NAP, MARD has established the National Steering Committee for Prevention and Control of Aquatic Animal Diseases, Antimicrobial Use and Antimicrobial Resistance in Aquaculture; issued 11 legal circulars on disease control, AMU and AMR; and issued more than 20 official letters to direct and enforce the control AMU and AMR. MARD has also organised several workshops and meetings between government agencies, companies, and associations to identify current problems, gaps, and difficulties in the control of AMU and AMR.

With regard to the control of veterinary drugs that are marketed in Viet Nam, MARD has requested the DAH and local agencies to inspect all importers (28 companies) for veterinary medicinal products and raw materials (especially for raw antibiotics) to identify how they are imported, used, and sold, and also to inspect veterinary drug shops to determine whether the antibiotic products that are sold are registered or non-registered. By law, all shops are now prohibited from selling raw antibiotic materials directly to farmers.

Awareness of Antimicrobial Resistance

To implement the activities of the NAP, the DAH has established collaborative programmes with the national television broadcasters (VTV1, VTV16) and newspapers to disseminate information on AMU and AMR, and has also conducted communication campaigns to increase awareness of AMR among farmers, drug sellers, and other stakeholders. Farmers have received instructions on proper AMU and key messages on AMR during surveys of AMU and AMR in shrimp, *Pangasius* catfish, tilapia, and traditional freshwater fish aquaculture. Technical staff, researchers, leaders, and managers have participated in national, regional, and international workshops and meetings on AMU and AMR to share and acquire experiences on how to improve awareness (such as participating in FAO project FMM/RAS/298/MUL and the Network of Aquaculture Centres in Asia-Pacific's (NACA) project on AMU in *Pangasius* catfish).

Surveillance

National programme on monitoring chemical/antibiotic residues on aquatic animals

MARD has approved, for every year since 2013, the national program on monitoring chemical/antibiotic residues in aquatic animals and their products. The monitored species include shrimp *Penaeus monodon* (Fabricius, 1798) and *Penaeus vannamei* (Boone, 1931), *Pangasius* catfish (*P. hypophthalmus*), tilapia *O. niloticus* , climbing perch *Anabas testudineus*, and snack-head fish *Channa striata* (Bloch, 1793). The parameters monitored include antibiotic and pesticide and chemical residues. Figure 1 shows the percentages of shrimp products that were positive for at least one antibiotic during the period 2013 to 2016.

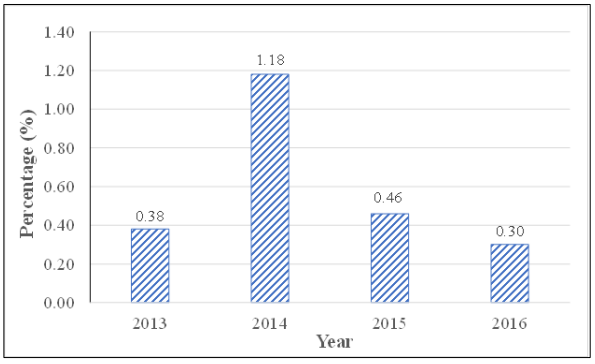

Fig. 1. Percentage (%) of shrimp products that were positive for at least one antibiotic during the period 2013–2016. No. of positive samples/no. of tested samples for each year were as follows: 2013: 09/2,365; 2014: 25/2,104; 2015: 08/1,751; and 2015: 06/1,692.

Pilot surveillance for AMU and AMR in Pangasius catfish aquaculture

During 2013–2014, MARD conducted pilot surveillance for AMR in *Pangasius* catfish aquaculture, sponsored by WHO. During this study, 75 catfish ponds belonging to six large catfish farms were sampled. The focus of the project was AMR in enteric (*Escherichia coli* and *Salmonella* sp.) and aquatic bacteria (*Aeromonas* spp. and *Vibrio* spp.) isolated from pond water, supply water, pond sediments, and catfish.

Survey on AMU in Pangasius catfish and shrimp aquaculture

During 2015–2016, through funding by the Government of Viet Nam, the DAH conducted a survey on AMU of 714 aquaculture households in three major *Pangasius* catfish production provinces (Ben Tre, Dong Thap, and An Giang provinces) and two major shrimp production provinces (Soc Trang and Bac Lieu provinces) (DAH, 2016). In 2017, DAH also carried out a survey on AMU in *Pangasius* catfish culture in Can Tho, An Giang, and Dong Thap provinces, sponsored by an FAO/NACA project.

Survey on AMU and AMR in tilapia and traditional freshwater fish

This survey was carried out by the DAH and Research Institute for Aquaculture No. 1 (RIA1) in 2017 under funding from project FAO/FMM/RAS/298. The objective of the survey was to assess the current status of AMU and AMR in the prevention and control of diseases in tilapia and traditional freshwater fish in two districts of Hai Duong Province (DAH, 2018). The survey design was developed using the principles and techniques of an epidemiological cross-sectional study and used a random multistage sampling method. Information and data on the production and disease situation in the culture of tilapia and traditional freshwater fish of Hai Duong Province were collected and used to develop the survey design. Two districts (Nam Sach and Ty Ky) having the highest density of tilapia production were selected for the survey (Fig. 2). A total of 60 households at six communes of these two districts were interviewed for information on AMU and AMR in November 2017.

Before implementing field activities, a one-day training course was organised in the surveyed province to provide local staff with background information on AMU and AMR. The training also included topics on the survey design, finalise the list of households to be interviewed, the standardised questionnaire, the methods for collection, management, and transportation of samples from the field to RIA1's laboratory; the detailed working plan and coordination of the field activities; and other logistic preparations. For each of the surveyed districts, a team was established to carry out field activities. At each selected household, the team

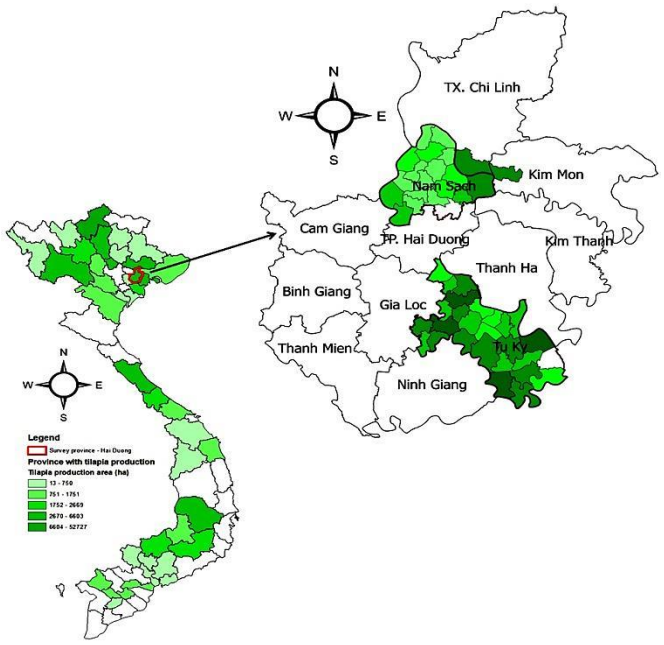

Fig. 2. Map of Nam Sach and Tu Ky districts in Hai Duong Province (red square) where the survey on the use of antibiotic and antibiotic resistance survey was conducted.

conducted a face-to-face interview with the owner to collect relevant information using 30 standardised questionnaire divided into three main parts: (1) baseline information about the household; (2) information on the household owner's knowledge on AMU and AMR; and (3) information on the owner's attitudes and practices regarding AMU and AMR.

A total of 177 samples (including 85 liver, 61 brain, 27 kidney and 4 mixes of liver and brain) were collected for isolation and identification of target pathogens (*Streptococcus* spp. and *A. hydrophila*). Also, in this study, a total of twenty *A. hydrophila* strains were further tested for AMR using 13 antibiotics (Table 1).

Table 1: Antibiotics used for antibiotic resistance testing of *Aeromonas hydrophila* strains.

No.	Antibiotic name
1.	Doxycycline (30 µg)
2.	Novobiocin (5 µg)
3.	Neomycin (30 µg)
4.	Rifampicin (30 µg)
5.	Florphenicol (30 µg)
6.	Chloramphenicol (30 µg)
7.	Trimethoprim/sulfamethoxazole (1.25/23.75 µg)
8.	Ciprofloxacin (5 µg)
9.	Oxacillin (1 µg)
10.	Erythromycin (15 µg)
11.	Streptomycin (10 µg)
12.	Tetracycline (30 µg)
13.	Vancomycin (30 µg)

For AMR analysis, isolates were categorised as wild type (fully susceptible, WT) or non-wild-type (NWT) using normalised resistance interpretation (NRI) determined cut-off values (COWT). Information derived from the AMU and AMR survey was entered into an MS Excel file which was linked with another one that consisted of laboratory test results and this combined data were used for descriptive analysis.

The results of AMU and AMR surveys in tilapia and traditional freshwater fish under the project FAO/FMM/RAS/298 as follows:

Production of tilapia and traditional freshwater fish: Descriptive analyses indicated that of the 60 investigated household owners, 78.3 % were male and 27.7 % were female (Table 2). As of November 2017, these owners had an average of 13.6 years of experience in the production of tilapia and traditional freshwater fish, with the longest having 29 years of experience and the youngest having only one year of experience. A majority (78.3 %) of the owners responded that they participated in one or more training courses on disease control, while 21.7 % said that they had never participated in any training courses. Most of the surveyed households (76.7 %) said that they cultured more than two species of tilapia and traditional freshwater fish in their production areas, while 23.2 % said that they cultured only one species (Table 2).

Knowledge about antibiotics: Although 95 % of the surveyed household owners said that they could detect aquatic animals with signs of disease, only 30 % of them had asked for technical advice on treatment. The majority (75 %) replied that they used antibiotics, although they could not differentiate well

Table 2. Baseline information regarding 60 households interviewed on the use of antibiotics and antibiotic resistant in aquaculture.

No.	Category	Number of households n = 60	Proportion of total number of households
1.	Gender		
	Male	47	78.3
	Female	13	27.7
2.	Year started fish culture	60	
	Oldest	1988	
	Newest	2016	
3.	Participated in training courses on disease control	60	
	Yes	47	78.3
	No	13	21.7
4.	Number of fish species cultured	60	
	Single	14	23.3
	Multiple	46	76.7

between antibiotics and other supplements such as vitamins and general mineral materials. Importantly, 65 % of the households said that they used a larger volume of antibiotics than that indicated in the instructions for use. This overuse could result in antibiotic resistance or imply that the quality of the antibiotics was not good enough. About 13.3 % of the households believed that antibiotics could be used to treat viral diseases, while 65 % said that they could be used to treat bacterial diseases. At least 16.7 % said that they used antibiotics to promote better growth.

Practices on using antibiotics: A majority (61.7 %) of the surveyed households said that they used antibiotics in compliance with manufacturer's instructions, and 78.3 % of them replied that they procured antibiotics from veterinary shops, compared with 11.7 % who said that sometimes they purchased antibiotics from both medical drug and veterinary drug shops. The reasons cited for the use of human antibiotics were cheaper cost and increased effectiveness. This is important information, as using antibiotics intended for human medicine likely results in AMR. Of the surveyed households, 38.8 % said that they received an introduction for the use of antibiotics from drug sellers, compared with 15 % who said that they did not have any information on usage. While 91.7 % said that they mixed antibiotics with food to feed fish, and 98.3 % of the surveyed households said that they considered various criteria (e.g. coverage, source, purpose of the antibiotic, expiry date, etc.) when buying antibiotics for their fish.

Bacterial isolation and AMR analysis: Among the 177 samples isolated for targeted pathogens, only two were positive for *Streptococcus* sp. and six were positive for *A. hydrophila*. Of these, two samples were collected from Nam Sach District and six were collected from Tu Ky District. The sampled fish did not show any clinical signs of disease. The isolated strains were identified as *A. hydrophila* and *S. agalactiae* based on their biochemical characteristics (Fig. 3).

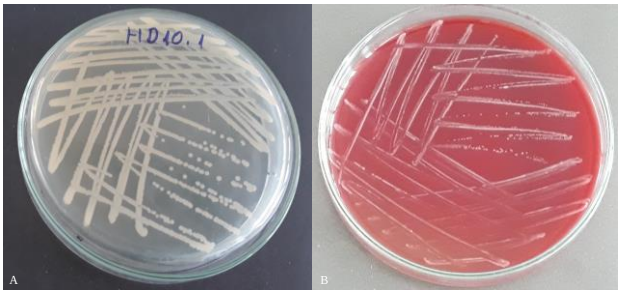

Fig 3. (A) *Aeromonas hydrophila* was isolated from tilapia (*Oreochromis niloticus*) collected in Hai Duong province in 2017; *(B) Streptococcus agalactiae* was isolated from climbing perch (*Anabas testudineus*) collected in Hai Duong province in 2017.

A total of 20 strains of *A. hydrophila* (including six strains isolated from this survey and 14 other strains isolated from tilapia and traditional freshwater fish in previous years) were tested for AMR (Table 3). The results showed that 45 % of the tested strains of *A. hydrophila* were non-wild type (NWT) for ciprofloxacin, 35 % were NWT for trimethoprim/sulfamethoxazole, 20 % were NWT for tetracycline and chloramphenicol, 15 % were NWT for erythromycin and doxycycline, 10 % were NWT for florphenicol and 5 % were NWT for rifampicin. Disc diffusions-based COWT were identified for WT of *A. hydrophila* strains as follows: ≥11 mm for florphenicol, ≥12 mm for erythromycin, ≥14 mm for rifampicin and neomycin, ≥18 mm for doxycycline, ≥19 mm for tetracycline and trimethoprim/sulfamethoxazole, ≥25 mm for chloramphenicol, and ≥34 mm for ciprofloxacin (Fig. 4).

Table 3. *Aeromonas hydrophila* strains used for antibiotic resistance testing.

No.	Bacterial strain	Host source	Year of isolation	Location (Province)
1.	*A. hydrophila* HDPT15.6	Tilapia (*Oreochromis noliticus*, Linnaeus, 1758)	2015	Phu Tho
2.	*A. hydrophila* CEDMA16.19	Tilapia (*O. noliticus*)	2016	Vinh Phuc
3.	*A. hydrophila* CEDMA16.20	Tilapia (*O. noliticus*)	2016	Vinh Phuc
4.	*A. hydrophila* CEDMA16.34	Tilapia (*O. noliticus*)	2016	Bac Ninh
5.	*A. hydrophila* CEDMA16.42	Tilapia (*O. noliticus*)	2016	Bac Ninh
6.	*A. hydrophila* HBTT16.01	Channel catfish (*Ictalurus punctatus*, Rafinesque,1818)	2016	Hoa Binh
7.	*A. hydrophila* CEDMA17.001	Spotted catfish (*Hemichromis guttatus*, Gunther,1862)	2017	Ha Nam
8.	*A. hydrophila* CEDMA17.002	Spotted catfish (*H. guttatus*)	2017	Ha Nam
9.	*A. hydrophila* CEDMA17.008	Tilapia (*O. noliticus*)	2017	Hoa Binh
10.	*A. hydrophila* CEDMA17.009	Tilapia (*O. noliticus*)	2017	Hoa Binh
11.	*A. hydrophila* CEDMA17.019	Channel catfish (*I. punctatus*)	2017	Hai Duong
12.	*A. hydrophila* CEDMA17.020	Tilapia (*O. noliticus*)	2017	Hai Duong
13.	*A. hydrophila* CEDMA17.021	Tilapia (*O. noliticus*)	2017	Hai Duong
14.	*A. hydrophila* CEDMA17.022	Grass carp (*Ctenopharyngodon idella*, Valenciennes, 1844)	2017	Bac Ninh
15.	*A. hydrophila* CEDMA17.044	Common carp (*Cyprinus carpio*, Linnaeus, 1758)	2017	Hai Duong
16.	*A. hydrophila* CEDMA17.045	Grass carp (*C. idella*)	2017	Hai Duong
17.	*A. hydrophila* CEDMA17.046	Grass carp (*C. idella*)	2017	Hai Duong
18.	*A. hydrophila* CEDMA17.047	Tilapia (*O. noliticus*)	2017	Hai Duong
19.	*A. hydrophila* CEDMA17.048	Grass carp (*C. idella*)	2017	Hai Duong
20.	*A. hydrophila* CEDMA17.049	Common carp (*C. carpio*)	2017	Hai Duong

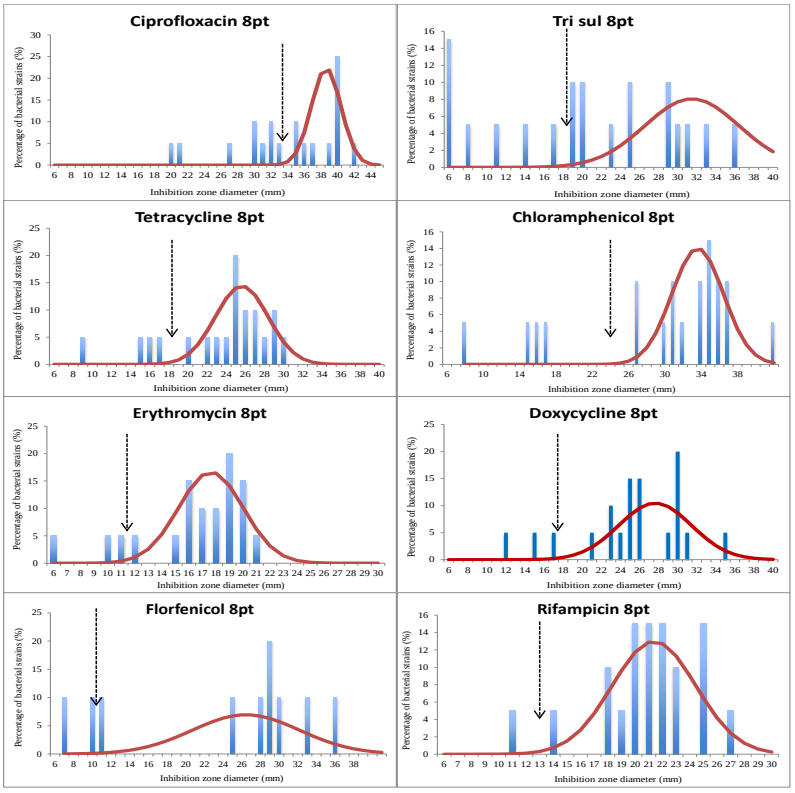

Fig. 4. AMR analysis of *Aeromonas hydrophila* strain isolated from tilapia *Oreochromis noliticus* and traditional freshwater fish common carp *Cyprinus carpio*, grass carp *Ctenopharyngodon idella*, silver carp *Hypophthalmichthys molitrix*, and climbing perch *Anabas testudineus*.

Best Practice

In terms of best practices, some national programmes for disease prevention and control have been established for main aquaculture species such as shrimp *P. monodon* and *P. vannamei* and catfish *P. hypophthalmus*, including national programmes for: (1) prevention and control of disease in *Pangasius* catfish, conducted between 2015 and 2020 (Decision 4995/QD-BNN-TY dated 20/11/2014) (MARD, 2014); (2) the establishment of disease-free compartments and zones for shrimp production (Decision 4088/QD-BNN-TY dated 01/10/2016) (MARD, 2016); and (3) for the active surveillance of diseases in shrimp and *Pangasius* catfish to be exported between 2017 and 2020 (Decision 1038/QD-BNN-TY dated 29/3/2017) (MARD, 2017b).

Annually, both national and local authorities issue national and local action plans for aquatic animal disease control and organise training activities on the principles of good antibiotic use in aquaculture. Best practices in shrimp, *Pangasius* catfish, tilapia, and other species have also been improved through the application of aquaculture technologies including VietGAP and GlobalGAP, and are encouraged through research and evaluation of alternative treatment measures to AMU (e.g. probiotic products, herbal/plant extract products).

Conclusion

Viet Nam has increased its capacity for the better management of AMU and AMR by using the One Health Approach. Several key activities have been implemented for the aquaculture component, such as awareness communication, training and education, legislation development, surveys to obtain basic information about AMU and AMR, applying best practices, and closely collaborating with international organisations such as WHO, OIE, FAO and NACA to implement activities on AMU and AMR. Because aquaculture is one of the most important sectors for economic growth in Viet Nam, the Vietnamese Government needs to continue implementing activities related to AMU and AMR in aquaculture in order to minimise the risk of AMR in the future.

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