



Aquaculture Component of National Action Plan on Antimicrobial Resistance in Malaysia

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Abstract

Antimicrobial resistance (AMR) is a serious and growing global public health threat. Given the grave importance of AMR, the United Nations General Assembly has called for the development and implementation of the national action plans (NAP) on AMR in each of its member countries. The Malaysia NAP was launched in February 2017 with collaborative approach from Ministry of Health, Ministry of Agriculture and Agro-based Industries [Department of Veterinary Services (DVS), Department of Fisheries (DOF), Department of Agriculture (DoA)], Department of Environment, Ministry of Higher Education, Ministry of Defence Hospitals, Private Healthcare Facilities, Community Pharmacist, The Animal Food Industry and Professional Organisations pertaining to Human And Animal Health) to address and mitigate AMR in respective sectors. This paper presents the aquaculture component of Malaysia's NAP on AMR lead by the DOF, Malaysia. The objective of this paper is to briefly present the outcomes of activities carried out by the DOF in relation to AMR and AMU in Malaysia which includes: i) the development of the aquaculture component of the NAP; ii) results of the AMU survey; iii) outcome of AMR surveillance; iv) AMR education and awareness; and iv) strengthening governance. The initial AMR results indicate that most of the *Escherichia coli* isolates were resistant towards erythromycin (90.7 %), cefepime (26.6 %), tetracycline (18.2 %), ampicillin (15 %), and chloramphenicol (10 %). On the other hand, the majority of the *Vibrio parahaemolyticus* isolates were resistant to ampicillin (72.3 %) followed by erythromycin (10 %), cefotaxime (4 %), and tetracycline (4 %).

Keywords: One Health, national action plan, fisheries, antimicrobial usage

Introduction

According to the World Health Organization (WHO), antimicrobial resistance (AMR) occurs when microorganisms (such as bacteria, fungi, viruses, and parasites) change when they are exposed to antimicrobial drugs (such as antibiotics, antifungals, antivirals, antimalarials, and anthelmintics). As a result, these medicines become ineffective and infections persist in the hosts, increasing the risk of spread to others. In 2016, Malaysia established a National Antimicrobial Resistance Committee (NARC) comprised of members from the human and animal health sectors under the One Health approach to develop the National Action Plan (NAP) on AMR. This was following the outcome of the 68th United Nations General Assembly in 2015 which urged all member

states to adopt the global action plan on AMR and to develop the country's NAP on AMR (WHO, 2015). The initial NAP framework outlines the views of stakeholders from across the sectors of human and animal health (including aquaculture) regarding the status, gaps, and solutions to address the AMR situation in Malaysia. This was continued with the development of the NAP, led by the Ministry of Health (MOH) and the Ministry of Agriculture and Agro-based Industries (MOA). The four main pillars of the NAP include: i) public awareness and education; ii) surveillance and research; iii) infection prevention and control; and iv) appropriate use of antimicrobials. The Malaysian NAP on AMR, or abbreviated as MyAP AMR, was officially launched by both the MOH and the MOA on 27 February 2018 in Putrajaya (Malaysian Action Plan on Antimicrobial Resistance (2017-2021), 2017). Among

the main roles of the Department of Fisheries (DOF) in the MyAP AMR are to: a) implement the survey on the status of antimicrobial usage (AMU) in the aquaculture sector; b) determine AMR properties of bacterial isolates obtained from fish, aquaculture facilities/ecosystems; and c) carry out awareness programs for the fish farmers on AMU and AMR.

The DOF's AMR aquaculture working group was established in April 2017 to carry out the implementation. At the same time, the DOF had also participated in the Project FMM/RAS/298/MUL: Strengthening capacities, policies and national action plans on the prudent and responsible use of antimicrobials in fisheries, which consists of workshops held in India (10–13 April 2017), Putrajaya (7–9 August 2017) and Singapore (12–14 December 2017) of the Food and Agriculture Organization of the United Nations (FAO). These workshops complemented the activities planned in MyAP AMR. The establishment of the governance mechanism for the NAP AMR (aquaculture component) in the DOF is represented in Table 1.

Status of Aquaculture in Malaysia

Aquaculture is now being promoted in Malaysia as an important engine of growth and a mainstay contributor to the nation's economy. Similar to many countries in the region, aquaculture in Malaysia serves to provide supplementary fish for national food security and production of high-value fish for foreign exchange earnings. Situated in a region with an abundant supply of land and water, two determinant factors for aquaculture activities, the Malaysia government has always strived to ensure that this sector is not sidelined in the country's development efforts.

According to the Annual Fisheries Statistics (2016), a total of 21,939 fish farmers and culturists were involved in the aquaculture industry. The majority (72.5 %) of the workforce was involved in the freshwater aquaculture sub-sector. The remaining 27.5 % of fish farmers/culturists were involved in the brackish-water aquaculture industry. In 2016, freshwater aquaculture contributed 103,348 tonnes valued at RM1,091,463 million. The main cultured species were freshwater catfish (*Clarias* sp.), black and red tilapia (*Oreochromis* sp.), riverine catfish (*Pangasius* sp.), and giant freshwater prawn (*Macrobrachium rosenbergii* Johnson, 1966). Brackishwater aquaculture production in 2016 contributed about 304,039 metric tonnes valued at RM2,509,717 million. The main cultured species were marine prawns (Tiger shrimp (*Penaeus monodon* Fabricius, 1798) and Whiteleg shrimp (*Penaeus vannamei* Boone, 1931)), cockles (*Tegillarca granosa* (Linnaeus, 1758)), grouper (*Epinephelus fuscoguttatus* (Forsskål, 1775)), red snapper (*Lutjanus argentimaculatus* (Forsskål, 1775)), and seabass (*Lates calcarifer* (Bloch, 1790)).

The DOF, Malaysia is the competent authority responsible for the implementation of the Fisheries Act (1985) which deals with the health of aquaculture animals and the prevention and control of aquatic diseases. In its role as the competent authority, the DOF carries out many functions which relate to the control of AMR including:

- Registration of aquaculture farms.
- Coordination of the national fish health surveillance programme.
- Public health monitoring programmes like the Sanitary and Phyto-Sanitary Programme for Aquaculture and the National Shellfish Sanitation Programme (NSSP).

Table 1. Steps taken in the establishment of a governance mechanism for Malaysia Action Plan on AMR (Aquaculture) in Malaysia.

Establishment of governance mechanism	Months in 2017											
	3	4	5	6	7	8	9	10	11	12		
a. Dialogue Session: AMR - Playing our part in combating the crisis (MOH, National Pharmaceutical Regulatory Agency, DVS, DOF, Federation of Livestock Farmers Association Malaysia)(Lead by MOH)		X										
b. Establishment of AMR (aquaculture) Working Group (DOF)		X										
c. Technical Working Groups (TWG) meetings		X	X									
d. AMR (aquaculture) Working Group Meeting (DOF)		X		X			X				X	
e. Present the NAP AMR (aquaculture) to the Department of Fisheries top management and endorsed (DOF)				X								
f. Co-ordination meeting of 4 TWGs on AMR and finalisation of National Action Plan on AMR (MOH)											X	
g. Development and formalisation of NAP AMR (which incorporates AMR (aquaculture))			X	X	X	X	X	X	X	X	X	X

- d. Development of fisheries biosecurity protocols.
- e. Assessment and management of imports, exports, and internal movements of live aquatic animals.
- f. Certification of fish farms – Malaysia Good Agricultural Practice(myGAP)(2014).
- g. Adoption of MS 1998:2007 – Good Aquaculture Practice (GAQP) – Aquaculture arm General Guidelines.
- h. Regular inspection on registered fish/shrimp farms by State Biosecurity Unit, DOF.
- i. Enforcing the Animal Feed Act (2009).

Purpose of the paper

The objective of this paper is to briefly present the outcomes of activities carried out by the DOF about AMR and AMU in Malaysia which includes: i) the development of the NAP AMR (aquaculture component) document; ii) results of AMU survey; iii) outcome of AMR surveillance; iv) activities on AMR education and awareness and iv) strengthening governance.

The Development of MyAP AMR

The MyAP AMR was officially launched by both the MOH and the MOA on 27 February 2018 in Putrajaya. The component on aquaculture is being included briefly in MyAP AMR. Hence the NAP AMR (aquaculture) is being prepared to include details specifically on AMR activities planned and implemented in the aquaculture sector in Malaysia. The first draft of the NAP AMR (aquaculture) is expected to be ready by June 2018. It is hoped that with this document, the activities regarding AMR will be more clearly defined, documented, and adhered to. The main activities carried out under the NAP AMR (aquaculture) are briefly presented below.

AMU Survey

Reports on AMU in Malaysia are very limited. The latest record is the report on the use of chemicals in aquaculture in Malaysia by Shariff et al. (2000), where a variety of antimicrobials used for treating fish and shrimp diseases in Malaysia are listed. Most of the antimicrobials used are generic imports from China and Thailand. Commonly used antibiotics include sulfonamides, tetracyclines, nitrofurans, chloramphenicol, oxolinic acid, and virginiamycin. Due to the long lapse of the available information in this area, a preliminary AMU survey was carried out by the DOF on 4th August 2017 at the Malaysia External Trade Development Corporation (MATRADE) during the AMR Awareness and Stakeholders Consultation organised together with the Malaysian Aquaculture Development Association (MADA). The session comprised of an awareness talk on AMR followed by an AMU survey. An AMU questionnaire adopted from FAO and the Network of Aquaculture Centers in Asia and the Pacific, with some modification, was used. A

total of 106 questionnaires were handed out to the participants. Out of this, only 46 respondents participated in filling the questionnaires which consisted of farmers (n = 28, 61 %), feed and drug suppliers (n = 12, 26 %), and aquatic animal health professionals (n = 6, 13 %). The results showed that only 8 out of 28 (28 %) farmers used antibiotics. Most of the farmers (19/28, 68 %) used other chemicals such as anti-helminthic and anti-parasitic drugs to treat fish infested with parasites. Commonly used antibiotics include oxytetracycline, erythromycin, and amoxicillin. Awareness of the approved or banned drugs, regulations on antimicrobial used in aquaculture, and guidelines for AMU in aquaculture were very limited among the farmers. The knowledge and experience gained during this exercise were used to improve the AMU surveillance program that continued until the end of 2018. The questionnaires have also been simplified. Face to face interviews will be adopted and more stakeholders (hatcheries, nurseries, grow out, ornamental fish farms, fish feed manufacturers) will be approached in future surveys.

AMR Surveillance

Under the MyAP AMR, the DOF focused on *Vibrio parahaemolyticus* and *Escherichia coli* as the target microorganisms to be studied for AMR surveillance. Both isolates are of importance to animal and public health. *V. parahaemolyticus* and *E. coli* isolates obtained from the DOF active surveillance program for the Sanitary and Phyto-Sanitary Programme (Aquaculture), the National Shellfish Sanitation Programme (NSSP), research and development undertakings, and diagnostic activities were used for AMR surveillance. The isolates were tested against 20 antibiotics of human and aquaculture interest. Bacterial isolation and antimicrobial susceptibility testing were carried out according to standard methods together with control culture in place. All the information regarding the sampling plan, sample preparation, bacterial isolation, and susceptibility testing methods are specified in the National Integrated AMR Surveillance Manual.

Bacterial isolation was executed at six DOF laboratories, namely: i) Fisheries Biosecurity Laboratory (FBL) Kuala Lumpur; ii) FBL, Bintawa, Sarawak; iii) FBL, Kuantan, Pahang; iv) FBL, Selangor; v) Fisheries Research Institute, Batu Maung, Penang; and vi) National Fish Health Division, Batu Maung, Penang. Antibiotic susceptibility pilot testing was done at the FBL in Kuala Lumpur. Table 2 provides the work plan for AMR surveillance that was carried out in 2017.

A total of 88 *E. coli* and 51 *V. parahaemolyticus* isolates, obtained from the DOF surveillance programmes from June to November 2017 were tested for antibiotic susceptibility testing. Details on the sources and origin of the isolates are given in Table 3. The initial results indicate that most of the

Table 2. Work plan for antimicrobial susceptibility testing conducted in 2017.

Activity/Month	Months in 2017									
	4	5	6	7	8	9	10	11	12	
a. Development of National Integrated AMR Surveillance Manual	X	X	X	X	X		2 nd Draft			
b. Preparation of laboratories to conduct AMR surveillance for <i>Vibrio parahaemolyticus</i> and <i>Escherichia coli</i>		X	X	X	X					
c. Bacterial isolation, identification, and confirmation		X	X	X	X	X	X	X		
d. Antibiotic susceptibility pilot testing in Fisheries Biosecurity Laboratory Kuala Lumpur							X		X	
e. WHONET* data entry and reporting to NARC									X	X

*WHONET is free Windows-based database software developed for the management and analysis of microbiology laboratory data with a special focus on the analysis of antimicrobial susceptibility test results.

Table 3. Sources of samples, type of samples, sampling location and number of bacteria isolates for AMR surveillance.

Bacterial isolates	Sources of samples (Jun–Nov 2017)	Type of samples	Sampling location	Number of isolates
<i>Escherichia coli</i> (n = 88)	Sanitary and Phytosanitary Programme (Aquaculture)	Catfish (<i>Pangasius</i> sp.) Tilapia (<i>Oreochromis</i> sp.)	Kedah, Melaka, Perlis, Kelantan, Negeri Sembilan	18
	National Shellfish Sanitation Programme (NSSP)	Green mussel (<i>Perna viridis</i> (Linnaeus, 1758)) Clams (<i>Geloina</i> sp.), Cockles (<i>Tegillarca granosa</i> (Linnaeus, 1758)), and freshwater bivalves (<i>Corbicula fluminea</i> (O.F. Müller, 1774))	Johor, Terengganu, Kelantan, Penang, Perak, Selangor, Kelantan	70
<i>Vibrio parahaemolyticus</i> (n = 51)	Sanitary and Phytosanitary Programme	Tiger shrimp (<i>Penaeus monodon</i> Fabricius, 1798)	Sarawak	4
	National Shellfish Sanitation Programme (NSSP)	Green mussel (<i>P. viridis</i>) Clams (<i>Geloina</i> sp.)	Sarawak	3
	R&D	Tiger shrimp (<i>P. monodon</i>) Whiteleg shrimp (<i>Penaeus vannamei</i> Boone, 1931)	Perak Selangor, Johor	8 14
	Diagnostic cases	Tiger shrimp (<i>P. monodon</i>) Whiteleg shrimp (<i>P. vannamei</i>)	Melaka, Kedah, Penang, Sabah, Perak, Sarawak	20
	Antibiotic Residue Monitoring Programme (ARMP)	Tiger shrimp (<i>P. monodon</i>)	Sarawak	2

E. coli isolates were resistant towards erythromycin (90.7 %), cefepime (26.6 %), tetracycline (18.2 %), ampicillin (15 %), and chloramphenicol (10 %). There was also a small percentage of resistance against colistin (7.3 %). On the other hand, the majority of the *V. parahaemolyticus* isolates were resistant to ampicillin (72.3 %). Resistance towards colistin was

the second-highest in *V. parahaemolyticus* isolates, followed by erythromycin (10 %), cefotaxime (4 %), and tetracycline (4 %). Susceptibility testing of *E. coli* and *V. parahaemolyticus* will be continued in 2018. The antimicrobial susceptibility testing of *E. coli* and *V. parahaemolyticus* isolates against colistin will be repeated with broth dilution assay method.

AMR Awareness and Education

One of the fundamental ways to address AMR in aquaculture is to ensure that fish farms adhere to the best practices for hygiene, biosecurity, and fish care and handling. This reduces the need for antimicrobials in the first place as does vaccinating fish to build their natural ability to withstand disease. To achieve this, the DOF must first improve the awareness and understanding of AMR through effective communication, education, and training. The first activity to initiate the campaign was to organise a series of awareness talks to the farmers, the extension staff of the DF, and the general public. The education and awareness programmes carried out by the DOF in 2017 are in Table 4 and Table 5.

In 2018, the DOF implemented more awareness talks and briefings to the farmers. In addition, the DOF prepared and printed simple, yet interesting posters on AMR and AMU distributed to farmers, drug suppliers and fish feed manufacturers in Malaysia. The DOF also published reports and articles relevant to AMR in fisheries and disseminated materials regarding the best practices.

Strengthening Governance Related to AMU and AMR in Food and Agriculture

The responsible use of veterinary medicines, including antimicrobials, in aquaculture in Malaysia, is governed by many regulations. The most relevant regulations are The Poison Act 1952 (Act No. 366) and Regulations, Poisons Regulation 1952, Feed Act 2009 (Act No. 968), Food Act (1983)(revision 2016) (Act No. 281), Fisheries Act (Act 317) (1985), Malaysian Quarantine and Inspection Services Act (Act 728) (2011), Feed Act (Act 968)(2009)[Section 53(2)(b), (c), (e), (f), (g) and (h)], Inland Fisheries and Aquaculture Enactment (2003) of Sabah State, Law of Sarawak, State Fisheries Ordinance (2003)[Chapter 54] and the latest being the Inland Fisheries Rules (Inland Aquaculture) 2017 (Section 29). Section 29 of the latest Fisheries Rules (Inland Fisheries Aquaculture) (2017), states that any licensee shall not use any aquaculture chemicals except with the approval of the Director-General of Fisheries and any licensee which contravenes this commits an offence.

Table 4. Education and Awareness programs conducted to develop awareness at the Competent Authority level.

Activity/Month	2017											
	3	4	5	6	7	8	9	10	11	12		
a. MyOHUN* National AMR Workshop, Putrajaya (6-9/3/17)	X											
b. FAO Workshop 1, Mangalore, India (10-13/4/17)		X										
c. MyOHUN National AMR Workshop, Faculty of Veterinary, University Putra Malaysia (UPM)(31/7-2/8/2017)							X					
d. FAO Workshop 2, Putrajaya, Malaysia (7-9/8/17)							X					
e. WHO Net Training (28-29/8/17)							X			X		
f. FAO Workshop 3, Singapore (12-14/12/17)												X

*Malaysia One Health University Network.

Table 5. Awareness building within the agriculture sector and activities undertaken to disseminate the information on AMR.

Activity/Month	2017											
	4	5	6	7	8	9	10	11	12			
a. Articles in Fisheries Bulletin (quarterly bulletin by DOF)			X					X				
b. A talk on AMR during Asia Pacific Aquaculture Conference 2017 (Farmers Day)(25/7/2017)				X								
c. A talk on AMR during Fisheries Biosecurity Strengthening Course (1-2 Aug 2017)						X						
d. AMR Awareness and Stakeholders Consultation (4/8/17)- Presented a talk and distributed a Fact Sheet on AMR						X						
e. Executive Talk: AMR in Fisheries						X						

In addition to the acts and regulations, there are also programmes such as the Fish Disease Surveillance Programme, Aquaculture Residue Monitoring Program (ARMP), Sanitary and Phytosanitary Aquaculture, and Malaysia Good Agricultural Practices (myGAP) Certification Programme that monitor, control, and encourage the prudent use of antimicrobials in fisheries.

The DOF also promotes the adoption of best practices in aquaculture, including the use of antimicrobials in aquaculture. This includes monitoring and improvement of protocols on the prudent use of antimicrobials and controlling the distribution of antimicrobials in aquaculture.

Research in vaccine development and on substitutes of antibiotics for use in aquaculture started in the year 2010. The Fisheries Research Institute under the DOF has invented a vaccine developed from a local *Streptococcus* isolate against *Streptococcus* infection in Tilapia (Ismail et al., 2016, Ismail et al., 2017, Sa'aidatun et al., 2018). This vaccine was named StrepToVax and filed as patent in 2015 (Certificate of Filing (COF) No: PI 2015702360). In addition, two herbal-based products SirehMAX (Patent No: MY-176273-A) and SitroPro (COF No: PI 20177031310) to treat bacterial infection and parasitic infestation in cultured marine fish have also been developed and are in the process of commercialisation.

Conclusion

The DOF still has a long way to go in assessing AMU and AMR status in Malaysia. The surveys need to be continued in obtaining data to ascertain the quantity of the antimicrobials used, their sources, and linkages between use and resistance frequencies observed. Participation in FAO workshops has given the DOF staff further information, knowledge, expert guidance, and some financial support to carry out preliminary AMU surveys. Furthermore, the DOF top management has been very supportive of the overall AMR planning and has given consent to proceed with AMR surveillance and training using the DOF's development fund. The activities carried out so far have managed to raise awareness on AMR at the fisheries/aquaculture sector level and enhance the knowledge and capacity of the competent authority.

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