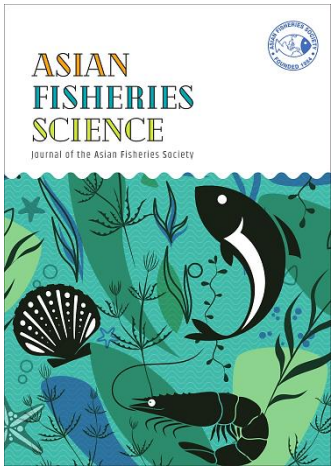

Review of National Residue Control Programme for Aquaculture Drugs in Selected Countries

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Abstract

Residues of drugs in aquaculture-raised products could potentially cause health hazards for consumers. Most seafood importing countries have regulations on maximum residue limits (MRL) for veterinary drugs in aquaculture products. National MRLs are generally based on Codex and where there are no Codex recommendations, countries may develop MRLs based on risk assessments. Most importing countries have regulations that require aquaculture-producing countries to demonstrate compliance by implementing a National Residue Monitoring Programme (NRMP). To understand the regulations and implementation of NRMP in seafood exporting and importing countries, an analysis was made on the regulations in Canada and EU and NRMP implementation in four major exporting countries; China, Viet Nam, Malaysia and Philippines. Data source were from websites of seafood inspection agencies in the countries and reports of inspection from EU Food and Veterinary Office (FVO). All seafood exporting countries have harmonised their regulations with that of EU and data on the implementation of NRMP is available from these countries. The regulatory pressure from the importing countries seems to drive NRMP implementation in the exporting countries.

Keywords: ASEAN, EU, maximum residue limit, regulatory

Introduction

The importance of aquaculture in meeting the growing demand for fish cannot be overemphasised. Presently, nearly half of global fish consumption comes from aquaculture (FAO, 2020). The rapid growth of aquaculture during the last two decades has not been without challenges. Mortality due to disease has been one of the greatest challenges and this has frequently been accompanied by the overuse of chemicals and drugs. The selection and spread of antibiotic resistance due to indiscriminate use of antibiotics in various sectors, including aquaculture, have been drawing the attention of agencies involved in public health as food safety regulators and consumers. The FAO/OIE/WHO expert consultation on antimicrobial use in aquaculture and antimicrobial resistance identified the following hazards associated with antimicrobial use in aquaculture (a) antimicrobial residues and (b) antimicrobial resistance (FAO/OIE/WHO, 2006). This paper mainly deals with antibiotic residues and risk management measures associated with this hazard.

Monitoring food commodities for the presence of chemical contaminants at a certain level is an important risk management measure that has been adopted by many countries for a long time. Modern food safety control programs are based on the principles of risk analysis. The Codex Alimentarius Commission (CAC) has guidelines for performing food safety risk analysis (CAC, 2018a). According to these guidelines, risk analysis has three major components: risk assessment, risk management, and risk communication. At the national level, national authorities are responsible for risk management. Generally, risk assessment requires a team of multidisciplinary scientists and data on the hazard and toxicological information. Risk management starts with risk evaluation, which includes identification of food safety issues and the development of risk profiles.

In the case of microbial hazards, a food safety issue may be brought to the attention of risk managers due to an outbreak of foodborne infection where the most adverse effects are acute and the result of a single exposure event (e.g. a meal of contaminated food). The level of the microorganism may go up or down in the food chain and contamination may even take place at various stages of the food chain. Whereas, chemical hazards such as residues of veterinary drugs, pesticides, and heavy metals, can cause adverse health effects due to the cumulative effect of multiple exposures. They are typically present at the primary production stage and their levels are not altered along the food chain. Therefore, when performing chemical risk evaluation, it is important to have information on the presence of the chemical hazard at the primary production stage.

Control of microbial hazards involves the implementation of measures in the food chain and the responsibility lies with those involved in the handling and processing of food. Conversely, control of chemical hazards involves the identification of fish farms where levels of hazards are above acceptable limits. This generally involves monitoring, testing, and implementing control measures to minimise the public health risk which is generally the responsibility of the national regulatory agencies.

Seafood industries have been using Hazard Analysis Critical Control Point (HACCP)-based food safety management. Certain antibiotics, such as chloramphenicol and nitrofurantoin, have been banned for use in food production animals. Detection of any residue of such banned antibiotics suggests a violation of the regulations. Certain antibiotics like tetracycline may be permitted for use for the treatment of bacterial diseases in aquaculture. The CAC has recommended maximum permissible limits for residues of such as antibiotics (CAC, 2018b). If any fish processing industry is using aquaculture products as raw material, antibiotic residues should be included in the list of possible hazards during the step of hazard identification. In the HACCP process, the critical control point would be at the reception of raw material to ensure that no contaminated fish enters the production chain. Data from farm monitoring would be helpful in sourcing raw material free of unacceptable residues.

Legislative Requirements

At the international level, the responsibility of providing advice on risk management concerning veterinary drug residues lies with the CAC and its subsidiary body, the Codex Committee on Residues of Veterinary Drugs in Foods (CCRVDF). The primary responsibility for risk assessment lies with the Joint FAO/WHO Expert Committee on Food Additives (JECFA). The CCRVDF determines the priorities for consideration of residues of veterinary drugs and JECFA provides independent scientific advice by evaluating the available data on veterinary drugs prioritised by CCRVDF. The Risk Assessment Policy for setting of MRLs in food established by the CAC, defines the responsibilities of CCRVDF and JECFA and their interactions. For the establishment of the priority list, CCRVDF identifies, with the assistance of member countries, the veterinary drugs that may pose a consumer safety problem and/or have a potentially adverse impact on international trade.

The JECFA uses a risk assessment process to establish an acceptable daily intake (ADI) and maximum residue limits (MRLs). Veterinary drugs that are toxic or have carcinogenic potential are not evaluated by JECFA and therefore no ADI or MRLs are established. Chloramphenicol and nitrofurans, compounds that caused disruptions in the trade of aquaculture products, belong to this category and are banned for use in food-producing animals in most countries. Presently, there are Codex MRLs only for chlortetracycline/oxytetracycline/tetracycline in fish and shrimp and flumequine in trout. The Codex MRLs exist for therapeutic agents used against parasites in salmon and trout aquaculture (e.g. deltamethrin, emamectin)(CAC, 2018b).

However, there are national/regional MRLs for several other antimicrobial agents. In the European Union (EU), the Commission Regulation (EC) No. 37/2010 establishes MRLs for veterinary drugs in foods of animal origin, including aquaculture products. The lack of Codex MRLs for veterinary drugs could be a problem for many developing countries that adopt Codex MRLs as national MRLs. This situation has led FAO/WHO (2004) to recommend that veterinary drugs which have been evaluated by national governments and are legally used in many countries, a comprehensive approach should be adopted to expedite harmonisation. The JECFA evaluation of substances may be constrained by the lack of data from companies that market the drug. FAO/WHO (2004) recommended that with the assistance of JECFA and based on national/regional MRLs, an initial list of temporary/operative MRLs could be adopted by CCRVDF. This list could be made permanent by CAC if the national/regional risk assessments are not questioned or if JECFA could establish the ADI using the data collected by the country/region to propose MRLs. Substances that do not fulfil these requirements could then be moved to the list of compounds not to be used in food animals. The CCRVDF has been working on a list of MRL needs of the member countries (what countries) and developed a database of MRL needs. The CCRVDF in its 23rd Session, held in Houston, Texas in October 2016, concluded that the Global Survey Database on MRL needs to be maintained and updated. The Committee established an Electronic Working Group to identify priority veterinary drugs and information gaps for a successful and comprehensive assessment by JECFA. The 85th meeting of JECFA, in Geneva, Switzerland from 24 October to 2 November 2017, re-

evaluated ampicillin and amoxicillin. Based on this evaluation, Codex has established MRL for amoxicillin and ampicillin in finfish fillet and muscle (CAC, 2018b).

For veterinary drugs without an ADI/MRL, regulatory authorities generally adopt a zero-tolerance approach. In this situation, as the analytical capability improves, the levels that were not detectable by earlier technology become detectable and hence reportable. Therefore, independent of any toxicological risk posed by the food product, the residues would attract regulatory action. The countries taking a zero-tolerance approach argue that the products are not acceptable because they have evidence of the use of a banned drug in animal production and therefore represent a violation of regulations. For example, in the EU, the misuse of banned antimicrobials is monitored using an analytical method that has a prescribed Minimum Required Performance Limit (MRPL). Liquid chromatography and tandem mass spectrometer (LC-MS/MS) are used to detect residues and the MRPL for chloramphenicol is 0.3 ppb and 1.0 ppb for metabolites of nitrofurans (EU regulation No EC 181/2003). A national residue control programme needs to be in place as per Council Directive No 93/26/EC and external countries wanting to export to the EU need to follow a sampling frequency based on the volume of production. The sample should consist of one or more fish depending on the size and the requirement of the analytical method. The minimum number of samples should be one per 100 tonnes of annual production.

In accordance with the EU guidelines, the substances to be monitored are divided into two groups: Group A includes substances having anabolic effects and unauthorised substances such as chloramphenicol and nitrofurans. Group B comprises of antibacterial substances, such as sulphonamides and quinolones, other veterinary drugs like anti-parasitic agents, and other substances and environmental contaminants including dyes, pesticides, and polychlorinated biphenyls (PCBs). Aquaculture products need to be monitored for the following groups of substances:

Group A: Substances having an anabolic effect and un-authorised substances:

- A1: Stilbenes, stilbene derivatives, their salts and esters
- A3: Steroids
- A6: Unauthorised substances. These include pharmacologically active substances for which no maximum limits can be fixed (chloramphenicol, nitrofurans)

Group B: Veterinary drugs and contaminants:

- B1: Antibacterial substances such as sulphonamides
- B2a: Antiheminthics
- B3a: Organochlorine compounds including PCBs
- B3c: Chemical elements
- B3d: Mycotoxins
- B3e: Dyes

One-third of the total samples are tested for Group A substances and two-thirds for Group B substances. The regulation further specifies that for Group A substances, samples should be taken at the farm level, at all stages of production, including fish that are ready to be placed on the market. For Group B substances, sampling should be carried out at the farm level, on fish ready to be placed on the market for consumption, either at the processing plant or at the wholesale level, and on fresh fish, on the condition that in the event a positive sample is detected, the sample can be traced back to the farm.

Table 1 presents information on the veterinary drugs considered by the Canadian Food Inspection Agency (CFIA) for residue monitoring. Drugs are grouped into approved (A) or banned (B). The fish species and the tissue in which the residue is to be monitored are specified. The residue levels at which would action would be taken are also indicated in Table 1.

Table 2 indicates the Canadian guidelines for malachite green in fish. As a minimum performance level of laboratory testing for Malachite Green (MG) or Leucomalachite Green (LMG), the laboratory must have a limit of quantification (LOQ) of at least 0.5 $ng.g^{-1}$ for MG or LMG. When the level exceeds 0.5$ng.g^{-1}$ but is below 1.0 $ng.g^{-1}$, the importers have the option of presenting evidence that there has been no deliberate use.

Gentian violet (GV) is not permitted in Canada for use during any part of the aquaculture fish production life cycle. Guidelines on regulatory action when the residue of GV or leucogentian violet is detected above 0.5 $ng.g^{-1}$ is indicated in Table 3.

The Association of Southeast Asian Nations (ASEAN), a regional organisation comprising of ten southeast Asian countries, have agreed on guidelines for the use of chemicals in aquaculture and measures to eliminate the use of harmful chemicals (ASEAN, 2013). Table 4 presents the regulatory status with respect of antibiotics in selected ASEAN countries.

Table 1. Residue monitoring in aquaculture products (Canadian Food Inspection Agency – CFIA).

Class name	Substance name (Marker residue / metabolite)	Use status	Species	Tissue	Action level (ppm)	Action level (ppb)
Amphenicols	Florfenicol (Florfenicol amine)	A	Salmonids	Muscle	0.8[a]	800[a]
	Chloramphenicol	B	All	N/A	DTC	DTC
	Thaimphenicol	NA	All	N/A	DTC	DTC
Avermectins	Emamectin benzoate	A	Salmonids	Muscle	0.1*	100*
	Ivermectin	NA	All	N/A	DTC	DTC
Benzoylureas	Teflubenzuron	A	Salmonids	Muscle Skin	0.3 3.2	300 3200
Fluoroquinolones	Ciprofloxacin, Danofloxacin, Enrofloxacin, Sarafloxacin	NA	All	N/A	0.001[b]	1.0[b]
Macrolides	Erythromycin	EDR	Fish Crustacean	Muscle	0.03[c]	30[c]
Nitrofurans	Furazolidone (AOZ), Furaltadone (AMOZ), Nitrofurantoin (AHD), Nitrofurazone (SEM)	B	All	N/A	DTC	DTC
Nitroimidazoles	HMMNI, IPZ, MNZ, RNZ, DMZ	B	All	N/A	DTC	DTC
Quinolones	Flumequine Oxolonic acid	B	All	N/A	DTC	DTC
Sulphonamides	Ormetoprim Sulphadiazine Sulphadi-metoxine	A	Salmonids	Edible tissue	0.1*	100*
	Trimethoprim	A	Salmonids	Muscle	0.1	100
Sulfonamides	Sulfacetamide Sulfadoxine Sulfachloro-pyridazine Sulfaguanadine Sulfamerazine Sulfamethazine Sulfamethiazole Sulfamethoxazole Sulfamethoxy-pridazine Sulfamono-methoxine Sulfamoxole Sulfanilamide Sulfapyridine Sulfaquinoxaline Sulfathiazole Sulfisoxazole	NA	All	N/A	DTC	DTC
Tetracyclines	Oxytetracycline	A	Salmonid Lobsters	Muscle	0.2	200
	Chlortetracycline Tetracycline	NA	All	N/A	DTC	DTC
Steroids	Boldenone (17 beta-boldenone) Methyl-testosterone (17 alpha-methyl-testosterone) Nandrolone (17 beta-19-nor-testosterone) Epi-boldenone (17 alpha boldenone) Epi-nandrolone (17 alpha 19 nor-testosterone)	NA	All	N/A	DTC	DTC
Stilbenes	Dienestrol Diethyl-stilbesterol Hexestrol	NA	All	N/A	DTC	DTC
Triphenyl-methane dyes	Gentian violet (Leucogentian violet) Malachite green (Leucomalachite green)	NA	All	N/A	See footnotes	See footnotes

A: Approved, B: Banned, NA: Not accepted to be used, N/A: Not applicable, DTC: Detected above the reporting limit, AHD: 1-Aminohydantoin hydrochloride, AMOZ: 3-amino-5-morphinomethy-oxazolidine-2-one, AOZ: 3-amino-2-oxazolidinone, DMZ: Dimetridazole, HMMNI: 2-Hydroxymethyl-1-methyl-5-nitroimidazole, IPZ: Ipronidazole, MNZ: Metronidazole, RNZ: Ronidazole, SEM: Semicarbazide.

* - Administrative maximum residue limit (AMRL), [a] – Fish will be considered rejected when the sum of florfenicol (parent drug) and florfenicol amine (metabolite) detected in the sample exceeds the florfenicol MRL, [b] – As a minimum performance level of the laboratories testing for fluoroquinolones, the laboratory must have a limit of quantification (LOQ) of at least 1.0 $ng.g^{-1}$ for fluoroquinolones, [c] – Interim action level set by Health Canada.

Table 2. Interim guidelines for product acceptability criteria for imported and domestic fish products (Health Canada and CFIA).

MG or LMG levels	Product action
≤0.50 ng.g^{-1} (interim LOQ for MG or LMG)	No regulatory action
>1.0 ng for MG or LMG	Product unacceptable. Importers have the option of gathering information to provide evidence of non-deliberate use. On a case-by-case basis, CFIA will take regulatory action
>0.5 ng.g^{-1} to <1.00 ng.g^{-1} for MG or LMG	Gathering of information required to determine deliberate use. The product is unacceptable unless a review of information shows there has been no deliberate use. Appropriate regulatory action will be taken as required

Table 3. Interim guidelines for the presence of gentian violet (GV) and leucogentian violet (LGV) as therapeutants and as possible contaminants (Health Canada).

GV or LGV levels	Product action
<0.5 ng.g^{-1} for GV and /or LGV (interim LOQ for GV or LGV)	No regulatory action
Sum GV and LGV >1.0 ng.g^{-1}	Product unacceptable
GV <0.5 ng.g^{-1} and LGV ≥0.5 ng.g^{-1} and <1.0 ng.g^{-1} OR GV ≥0.5 ng.g^{-1} and <1.0 ng.g^{-1} and LGV <0.5 ng.g^{-1}	This result will trigger a follow-up investigation for possible therapeutant use before making a decision
GV ≥0.5 ng.g^{-1} and LGV not detected at reporting level	This result will trigger a follow-up investigation for possible postharvest contamination before making of decision

Table 4. Regulations for antibiotics in selected ASEAN member countries.

Antibiotic/ Chemotherapeutic Agent	Malaysia	Philippines	Viet Nam
Tetracycline	Permitted	Permitted	Not used
Oxytetracycline	Permitted	Permitted	Permitted
Doxycycline	No data	Permitted	Permitted
Chlortetracycline	Permitted	Permitted	Not used
Nitrofurans	Prohibited	Prohibited	Prohibited
Chloramphenicol	Prohibited	Prohibited	Prohibited
Oxolonic acid	Permitted	Permitted	Not used
Erythromycin	Permitted	Permitted	Not used
Sulfonamides	Permitted	Permitted	Permitted
Sulfamerazine	Permitted	Permitted	Permitted
Amoxycillin	Permitted	Permitted	Not used
Enrofloxacin	No data	Permitted	Prohibited
Florfenicol	No data	Permitted	Permitted
Norfloxacin	No data	Permitted	Not used
Rifampicin	No data	Permitted	Not used
Ciprofloxacin	No data	No data	Not used
Sarafloxacin	No data	No data	Not used
Ormethoprim	No data	No data	Permitted
Sulphadimethoxin + Ormethoprim	No data	No data	Permitted
Sulphadimethoxin + Trimethoprim	No data	Permitted	Permitted
Metronidazole/ Dimetronidazole	Prohibited	Prohibited	Prohibited
Acriflavine	Permitted	No data	Not used
Trichlorofon	Permitted	Permitted	Not used
Trifluralin	Not used	Permitted	Prohibited
Cypermethrin	Not used	Permitted	Permitted
Praziquantel	Permitted	Permitted	Permitted
Levamisole	Not used	Not used	Permitted

Implementation of the National Residue Control Plan (NRCP) in Selected Countries

China

Since China is a major exporter of aquaculture products to the EU, the NRCP in China is largely harmonised with that of the EU. The EU Food and Veterinary Office (FVO) has been carrying out audits of the fish inspection system being implemented in China and reports of FVO audits provide information on the implementation of the NRCP (FVO, 2006, 2009, 2013). The Ministry of Agriculture and Rural Affairs (MARA) and the General Administration of Quality Supervision, Inspection, and Quarantine of the People's Republic of China (AQSIQ) are involved in planning, supervision, and follow-up of the annual NRCP. The AQSIQ is responsible for all the exported commodities while the MARA is principally responsible for the control and supervision of the domestic market. The MARA is also involved in sampling and follow-up of non-compliant results on farms that are approved under the Export Oriented System (EOS). The AQSIQ officials collect the majority of the samples in EOS farms. Each year AQSIQ and MARA hold three coordinating meetings for the planning of the prospective NRCP. The information on the NRCP results, experiences obtained during the previous year, and suggestions are sent from the MARA and China Inspection Quarantine (CIQ) provincial authorities to their respective Central Authorities at the beginning of the year. The MARA and AQSIQ each develop a separate NRCP, taking into account the input of their respective local authorities. The combined NRCP for the year is finalised by the end of March and includes the two different plans of the MARA and AQSIQ. China has harmonised its NRCP with EU requirements and sampling is planned based on usage data (Fig.1).

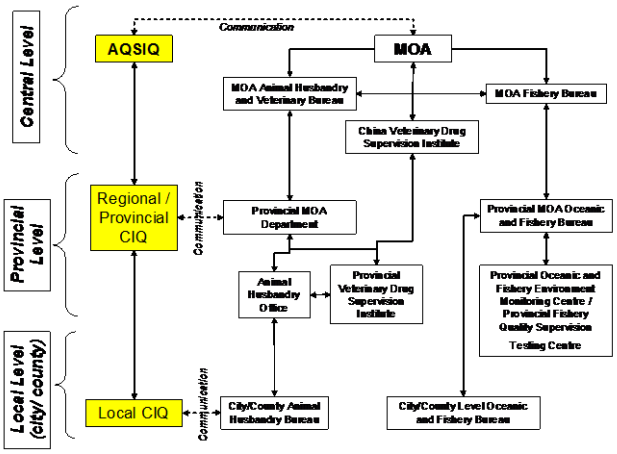

Fig. 1. Organisational structure of general administration of quality supervision, inspection, and quarantine at the Ministry of Agriculture of the People's Republic of China.

Follow-up procedures are issued from AQSIQ to the provincial CIQs via its annual NRCP. These procedures communicate that samples should be analysed and reported within 30 working days by the laboratory. In the event of a non-compliant screening result, the analysis is required to be confirmed within a week. The final confirmed result is transmitted to the sample submitter who will inform the sample taker and the farm/establishment of origin within 48 hours. An investigation should be carried out on the farm with two additional follow-up samples, which should be analysed within 10 days. If this result is non-compliant, the approval for the export of this establishment is revoked and corrective measures must be taken.

General follow-up instructions are also issued from MARA to their provincial authorities via its annual NRCP. The procedure communicates that five additional samples should be taken in case of a non-compliant result and that an investigation must be performed.

Some of the AQSIQ laboratories have been designated National Reference Laboratories (NRLs) for certain substances. NRLs are responsible for one or more substance groups that may carry out confirmatory analysis when the routine laboratory has no method for confirmation and are required to organise proficiency tests and give training and technical advice to the control laboratories within their respective networks. All AQSIQ laboratories are accredited to ISO 17025 by the Chinese National Accreditation body (CNAL). The laboratories in the network are well equipped and their quality assurance systems generally contain the essential elements such as a quality manual, standard operating procedures, equipment calibration records, internal standards, and analytical standard management. CNAL is a member of the International Laboratory Accreditation Cooperation. According to the EU FVO audit report (FVO, 2009), there are a total of 106 laboratories administering the 2009 NRCP. Of these, 71 are in the MoA network (of which are reference laboratories) and 35 are within the AQSIQ network (8 of which are reference laboratories).

The Food Safety Law of the People's Republic of China, which was established on 1 June 2009, requires all food producers and traders to establish a food safety management system, to inspect and test foods produced including raw materials, food additives, and to allow the release of the products only after successful inspection. Some of the ISO 17025-accredited processing establishments may be using Enzyme-Linked Immunosorbent Assay (ELISA) for screening, but some establishments including feed manufacturing units have LC-MS/MS systems which can reach the required level of sensitivity. There is a comprehensive national legal framework governing the manufacture, authorisation, sale, and distribution of veterinary medicinal products in China. National

MRLs have also been established (MoA Order 235) and withdrawal periods for pharmacologically active substances are specified in the MoA Order 278 of 22 May 2003. Off-label use is not permitted in Chinese regulation. China has also banned the use of certain veterinary medicinal products (Article 39, Chapter 6 of the Regulation on the Administration of Veterinary Drugs). Lists of banned drugs have been published (MoA Orders No 193, 560, 176, 265, and Joint MoA/State Food and Drug Administration Order No 227).

According to the MoA, veterinary medicinal products may be distributed from manufacturers/importers to qualified and licensed veterinary drug practitioners and end-users (e.g. feed mills or farms with a veterinarian on-site). Veterinary medicinal products may also be sold by qualified and licensed vendors? to end-users (e.g. farmers). The administrative department for veterinary medicine of the local people's governments at or above the county level (i.e. the Veterinary Livestock Bureau at County Level) administers the licensing system for veterinary medicinal product retailers. Licensed retailers must comply with the Good Sale Practice for veterinary medicinal products established by the administrative department for veterinary medicine of the State Council and comply with the measures for the administration of veterinary prescription drugs. Qualified veterinary drug practioners must have competent technical personnel appropriate for their veterinary drug practice. They must have fixed premises, equipment, and storage facilities for business and must also have obtained a veterinary drug practitioner certificate and the business license issued by the industry and commerce authority. Not all veterinary medicinal products for use in food-producing animals are classified as "prescription only" since some are available over-the-counter (FVO, 2009).

Malaysia

The Fisheries Biosecurity Division of the Department of Fisheries of Malaysia is responsible for developing, monitoring, evaluating, auditing, and compiling records of the Aquaculture Residue Monitoring Programme (ARMP). As per EU regulation, the minimum number of samples to be collected is maintained at one per 100 tonnes of production. One-third of the total samples are tested for Group A substances and two thirds for Group B substances. Standard Operating Procedure for the ARMP is available with the Fisheries Biosecurity Division and this specifies that the selection of commodity-matrix-residue combination for inclusion in residue monitoring would be based on a risk profile that considers several factors including:

- Use of a particular chemical or veterinary drug;
- Likelihood of the occurrence of residue;
- Extent of use, usage pattern, and incentives for misuse;
- Extent to which the residue has been monitored in the past and the results of that monitoring;
- Specific market access requirements and the perception of the residue as a possible health hazard.

While the minimum samples to be collected are based on EU regulations, samples collected at the farm level cover a minimum of 10 % of registered farms. The number of samples for each will be taken/collected by staggering months and the Fisheries Biosecurity Division shall determine these timelines. Sampling is on a random basis and covering all registered farms, including those exporting products to the EU market and farm locations being monitored for sanitary and phytosanitary (SPS) compliance. Tables 5 and 6 provides data on number of samples of shrimp and finfish collected and number of samples analysed for different veterinary drugs. All samples are not analysed for all drugs and the Biosecurity Division uses the risk profile criteria mentioned above to decide on the veterinary drug to be analysed in a particular sample.

The following species are covered based on their annual production:

- Black tiger shrimp (*Penaeus monodon* Fabricius, 1798)
- Pacific white shrimp (*Litopenaeus vannamei* Boone, 1931)
- Giant freshwater prawn (*Macrobrachium rosenbergii* (de Man, 1879))
- Seabass (*Lates calcarifer* (Bloch, 1790))
- Tilapia (*Oreochromis* sp.)
- Grouper (*Epinephelus* sp.)
- Snapper (*Lutjanus* sp.)
- Silver pompano (*Trachinotus* sp.), and
- River catfish (*Pangasius* sp.)

The laboratories performing analysis have ISO 17025 accreditation. The turnaround time in the laboratory is 14 days.

To improve food safety and aquaculture production that does not go to the EU market, Malaysia introduced the SPS programme in 2011. The number of samples analysed for residues of veterinary drugs from farms covered under the SPS programme was 60 in 2011, 325 in 2012, and 105 in 2013.

Table 5. Samples collected for residue monitoring under the aquaculture residue monitoring programme (ARMP) during 2008–2013.

Year	Shrimp	Finfish
2008	562	213
2009	505	299
2010	574	448
2011	806	599
2012	918	744
2013	710	770

Table 6. Number of shrimp and finfish samples analysed for various veterinary drugs under aquaculture residue monitoring programme (ARMP).

Parameter	2008	2009	2010	2011	2012	2013
Shrimp						
Chloramphenicol	79	45	60	80	100	70
Nitrofurans	67	45	55	80	100	80
Nitroimidazoles	22	35	55	70	100	80
Antibacterials	128	123	180	250	300	230
Antihelmenthics	68	64	70	100	120	100
Dyes	68	25	25	40	45	35
Finfish						
Stilbenes	18	23	50	65	80	80
Steroids	16	23	50	65	80	80
Chloramphenicol	40	20	15	25	30	25
Nitrofurans	30	17	20	25	30	30
Nitroimidazoles	22	16	15	20	20	25
Antibacterials	84	74	150	200	240	250
Antihelmenthics	39	29	60	80	100	100
Dyes	26	16	25	35	40	35

Philippines

The Philippines is implementing an NRCP that is in line with international market requirements despite several limitations. The Fish Health Management and Quality Assurance Section (FHMQAS) of the Bureau of Fisheries and Aquaculture Resources (BFAR) have the responsibility of implementing the NRCP in the Philippines. The NRCP in the country includes:

- Aquaculture farm registration system;
- Monitoring hygiene of production;
- Disease surveillance and reporting;
- Dissemination of information and education of aquaculture food chain operators on the need for aquatic animal feeds, veterinary drugs, and product registration before their marketing and usage;
- Surveillance and monitoring of aquatic animal feeds, veterinary drugs, and products by the Aquatic Animal Feed and Veterinary Drug and Product Control Officers;
- Regulatory action on any violation of policies and guidelines on registration, manufacturing distribution, and use of veterinary drugs and aquatic animal feeds;
- Assistance in planning, directing, and supervising the national programme on aquatic feeds, veterinary drugs, and product control.

Many administrative orders and decisions form the legal basis for the NRCP. These include Fisheries

Administrative Orders (AO), Fisheries Office Orders (FOO), General Memorandum Order (GMO), and Department of Agriculture Administrative Order (DA-AO) which are indicated below:

- Fisheries AO No 210 series of 2001- Regulations for the exportation of fresh/chilled and frozen fish and fishery products.
- Fisheries AO No 212 series of 2001- Guidelines on implementation of HACCP systems.
- Fisheries AO No 21 series of 2003- Amendment of Fisheries Office Order 147-01, Series of 2001: Designation of Regional Fish Health Officers of BFAR.
- FOO No. 210 Series of 2003 - On-farm residue monitoring.
- GMO No 225 Series of 2004 – Continued implementation of Commission Decision 2003/858/EC by Fish Health Officers.
- Memorandum Circular Order No 01, Series of 2005- Sanitary and Phytosanitary requirements for exportation of aquaculture products for quality assurance and food safety.
- Special Order 310, Series of 2005 – Designation of Fish Health Section as the National Reference Laboratory for Veterinary Residues for Aquaculture Products.
- FOO No. 155, Series of 2005 – Creation of the Fish Inspection and Quality.

Assurance Service (FIQAS); FOO No. 152, Series of 2005 – Creation of Fishery Inspection and Quality Assurance Service: Residue Monitoring and Disease Surveillance;

- FOO No. 247, Series of 2006 – Powers and Functions of Regulatory Officers (Fish Inspectors, Fish Health Officers, Fisheries Quarantine Officers, and Certifying Officers) for Safety and Quality Assurance of Fishery and Aquaculture Products Intended for Human Consumption;
- DA-AO No. 24, Series of 2009 – Implementing Guidelines on the National Veterinary Drug Residues Control Program in Food according to Administrative Order No. 14, Series of 2006;
- DA-AO No. 14, Series of 2006 – Implementation of the National Veterinary Drug Residues Control Program and Creation of the Inter-agency Committee.

The NRCP implementation was also strengthened under DA-AO No. 14, Series of 2006, on the implementation of the national veterinary drug residues control programme and the creation of an inter-agency committee, and DA-AO No. 24, Series of 2009, as its implementing rules and regulations. This defines the roles of the competent authority, farmers, and suppliers. The fish health officers of BFAR are deputised as Aquatic Animal Feed and Veterinary Drug and Product Control Officers through DA Special Order No. 23, Series of 2002 and Special Order No. 69, Series of 2004, to conduct inspection and sampling at aquaculture facilities, fish ports, fish processing plants, and markets to monitor the use of veterinary drugs and products in aquaculture. The application of restricted veterinary drugs requires a prescription by a duly licensed veterinarian and their use must comply with the applicable regulations, particularly for drugs requiring a minimum withdrawal period.

The following products have been banned through joint DOH and DA Administrative Orders (AOs):

- Beta-agonist: DA AO No. 14, Series of 2003 – Ban on the Use in Food Animals of Beta-agonist Drugs Used in Humans as Bronchodilators and Tocolytic Agents.
- Nitrofurans: DOH and DA Joint AO No. 2, Series of 2000 – Declaring a Ban/Phase-Out of the Use of Nitrofurans in Food-Producing Animals.
- Olaquindox and carbadox: DOH AO No. 4-A and DA AO No. 1, Series 2000 – The Banning and Withdrawal of Olaquindox and Carbadox from the Market.
- Chloramphenicol: DOH AO No. 91 and DA AO No. 60, Series of 1990 – Declaring a Ban on the Use of Chloramphenicol in Food-Producing Animals.

The designated fish health officer collects samples from farms supplying raw materials to accredited exporters. A representative sample of 1 kg (pooled sample) is collected from the farm. The sample label would contain information such as sample code, date of collection, name of the farm, pond number, days of culture, feed being used, and the analysis to be performed. Table 6 shows the limit of detection, limit of quantification and maximum detection limit for residues of chloramphenicol and metabolites of nitrofurans in the Philippines. Once the analysis is completed, copies of the results are sent to FIQAS for issuing a health certificate and another copy is given to the farmer. In the case of feed, duplicate samples of 250 to 500 g are collected from each representative bag and the sample label would contain information on the date, kind, brand name, and name of the miller. The samples are sealed and labelled in front of the manufacturer/distributor and a duplicate sample is given to the miller/manufacturer. A copy of the results of the analysis is also provided to the miller/manufacturer. In the case of products, 1 kg of the sample is collected and information on the farm

which produced the raw material and the country destination of the product is recorded on the label. The results of the analysis should be provided within 3 to 4 days of sample collection.

The Central Fish Health Laboratory is the National Reference Laboratory for residues of veterinary drugs. In addition to BFAR Regional laboratories, the services of two private laboratories in Manila and General Santos, are used for residue monitoring.

Viet Nam

In Viet Nam, the Department of Aquaculture (DOA) is responsible for controlling the production, distribution, and use of feeds. The Department of Animal Health (DAH) is responsible for controlling the production, distribution, and use of veterinary medicinal products. The National Agro-Forestry-Fisheries Quality Assurance Department (NAFIQAD) is responsible for the planning and implementation of residue control plan, including follow up. The legal basis for the residue control programme has been harmonised with the requirements of EU Directive 96/23/EC as recorded in the 2003 report of the audit by the EU FVO. Viet Nam has been implementing NRCP, while reviewing and improving the programme continuously. The FVO audit report of 2003 indicates that NAFIQAD has well-equipped laboratories and well-trained manpower to carry out residue monitoring as a requirement under the EU legislation. Some of the shortcomings noted in this report are inadequacy of legislation to ensure that veterinary medical products approved for other animal species are not used in aquaculture. In addition, rules need to be in place regarding the use of veterinary medicines through the feed. Regardless, the improvements made are evident from the fact that in 2001 Viet Nam received 20 Rapid Alert System for Food and Feed (RASFF) notifications for chloramphenicol (CAP) in crustaceans and received 34 RASFF notifications for CAP in crustaceans and two in fish in 2002. These RASFF notifications were reduced to three in shrimp and one in fish in 2003. Data in Table 7 indicates that while RASFF notifications for CAP have been subsequently low, new problems arose due to malachite green. There were eight RASFF notifications for this dye in 2004, which increased to 30 in 2005 and came down to eight in 2006 and four in 2007. The FVO audit report noted that further improvements have been made in NRCP and most of the deficiencies pointed out in the 2003 report have been addressed by NAFIQAD. The number of samples to be collected is based on the EU requirement of one sample per 100 tonnes of production. The NAFIQ prepares a sampling plan based on data from the previous year, test reports from importing countries, substances authorised for use in aquaculture in the country, and information on the use of veterinary medicines. The Ministry approves the plan at the beginning of the year. During implementation, local authorities select sites based on production, information on the use of veterinary medicines, harvest period, and occurrence of diseases. Decision No. 130/2008/QD-BNN of 31 December 2008 of the Ministry of Agriculture and Rural Development forms the main legal basis for the residue-monitoring programme in Viet Nam. Four appendices to Circular 15/2009/TT-BNN established which chemicals, drugs, and antibiotics are either prohibited or authorised for use in manufacturing and trading in aquaculture. Further amendments to the list have come through circulars e.g. Circular 20/2010/TT-BNNPTNT of 2 April 2010 adding trifluralin to the prohibited list, Circular 03/2012/TT-BNNPTNT of 16 Jan 2012 adding cypermethrin, deltamethrin, and enrofloxacin to the prohibited list. Commercial production of medicated feed is prohibited, though farmers may add veterinary medicinal products to the feed using their mixers.

The NAFIQAD website provides details of the NRCP plan and data from 2009 onwards. This is illustrated in Tables 8 and 9. Generally, the planned numbers of samples are collected. The numbers of samples that fail to meet the requirements are also indicated in Table 10. In addition to the NRCP, Viet Nam has been carrying out extensive pre-export testing for banned veterinary medicines, CAP, nitrofurans, and malachite green since 2005. A minimum of two samples per batch of aquaculture products are collected by local authorities and tested. These measures resulted in a significant drop in the number of RASFF notifications after 2005. The 2009 Mission Report of EU FVO noted that Vietnamese authorities make some adjustments in sample numbers based on cultural practices. For crustaceans farmed in intensive farms, sampling is conducted per EU regulations (i.e. one sample per 100 tonnes of production). But for semi-intensive farms, testing is focused on the contaminants in EU regulation (Group B3) and samples drawn are less than 1 per 100 tonnes (e.g. 1,740 samples tested from 245,908 tonnes of production). In the case of fish grown in super-intensive systems (300–500 tonnes.ha^{-1}), sampling is usually one per pond (of 500 tonnes of production), e.g. 1,751 samples taken from 915,082 tonnes of production. Group A6, which includes banned antimicrobials, is tested at all stages of production. The scope of pre-export testing was redefined through Decision No. 1471/QD-BNN-QLCL of 20 June 2012 to include enrofloxacin and trifluralin in addition to chloramphenicol, nitrofurans, malachite green, and leucomalachite green. Additionally, processors should make internal checks before procuring raw material and this may include chlorpyriphos and flumequine in the test panel (EU FVO Report 2012).

The NAFIQAD Branch No. 4 is the National Reference Laboratory for fisheries products and receives samples from other laboratories. This laboratory is well equipped and is accredited to ISO 17025 for all the analyses.

Table 7. Detection of nitrofurans and chloramphenicol using ELISA by the Philippine Bureau of Fisheries and Aquatic Resources.

Limit	Chloramphenicol		Nitrofurans	
	Fish and fishery products	Aquatic feeds	Fish and fishery products	Aquatic feeds
Limit of detection	0.05 ppb	0.2 ppb	0.1 ppb	10 ppb
Limit of quantification	0.15 ppb	0.6 ppb	0.3 ppb	30.0 ppb
Maximum detection limit	4.05 ppb	16.2 ppb	8.1 ppb	81.0 ppb

Table 8. Number of rapid alerts due to residues of antibiotics and dyes in aquaculture products from Viet Nam during 2001-2016.

	Number of rapid alerts during years during 2001-2016															
	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Chloramphenicol	20	36	4	4	1	3	0	0	2	2	1	1	0	2	2	
Nitrofurans	0	12	0	2	1	1	1	1	0	2	5	0	0	5	5	5
Quinolones	0	0	0	2	2	1	0	0	0	0	0	0	0	0	0	0
Tetracyclines	0	0	0	0	0	0	0	0	0	0	0	0	2	22	4	6
Malachite green	0	0	0	8	30	8	4	1	2	2	2	0	1	0	3	0
Others	0	0	0	0	0	0	0	0	0	0	0	1	0	2	4	1

Table 9. Number of samples tested for residues of antimicrobial agents in Viet Nam.

Species	2009	2010	2011	2012	2013	2014	2015
Pangasius sp.		1474	1265	1378	1194	766	733
Tilapia (*Oreochromis* sp.)		60	98	211	175	181	168
Anabas (*Anabas* sp.)		26	45	49	20	12	4
Channa micropeltes (Cuvier, 1831)		52	34	69	46	56	71
Penaeus vannamei Boone, 1931		1338	731	829	1268	1430	1193
Penaeus monodon Fabricius, 1798		804	945	1300	1082	661	491
Macrobrachium rosenbergii (de Man, 1879)		35	24	22	15	13	17
Scylla serrata (Forskål, 1775)		12	13	13	16	15	18
Fishery raw material		134	141	161			
Hatchery water		140	202	192			
Featherback (*Notopterus* sp.)			20	9			4
Grass carp (*Ctenopharyngodon idella* (Valenciennes, 1844))			6	5			
Four-eyed sleeper fish (*Bostrychus sinensis* Lacepède, 1801)			7	3			14
Sea bass (*Lates calcarifer* (Bloch, 1790))							12
Total		4075	3531	4241	3830	3134	2719

Conclusion

Residue monitoring in most of the aquaculture producing countries is driven by international market requirements. As a single trading block, the EU accounts for over 60 % of imports, and the regulations in EU member countries are consistent and uniform. Therefore, many aquaculture-producing countries strive to comply with EU requirements. For chemicals banned for use in aquaculture, the EU follows the approach of using the most sensitive method available for detection and the regulations

Table 10. Number of tested samples and non-compliant samples in Viet Nam.

Substance tested	MRL	2009	2010	2011	2012	2013	2014	2015
Diethylstilbestrol	ND	0/51	0/58	0/72	0/64	1/62	0/50	0/49
Methyltestosterone	ND	0/53	0/55	0/74	0/62	2/65	0/51	0/50
Chloramphenicol	ND	05/887	3/742	1/511	2/669	0/731	1/396	3/367
HMMNI, IPZ, IPZ-OH, MNZ, MNZ-OH, RNZ, DMZ		NT	NT	NT	NT	0/25	7/196	1/153
AOZ	ND	0/883	1/765	1/526	0/948	0/699	0/338	0/329
AMOZ	ND	0/883	3/765	0/526	0/948	0/699	0/338	0/329
AHD	ND	0/883	4/768	4/526	0/948	0/699	0/338	0/329
SEM	ND	07/888	3/766	3/526	0/948	0/699	0/338	0/329
Tetracyclines								
Chlortetracycline	100	0/258	0/185	0/56	0/165	0/215	NT	NT
Oxytetracycline	100	0/258	0/185	1/149	2/165	4/215	1/247	2/219
Tetracyclines	100	0/258	0/185	0/149	0/165	NT	0/247	0/219
Doxycycline	100	NT	NT	NT	NT	1/30	3/247	0/219
Sulphonamides								
Sulphadimethoxine	100	0/697	0/577	0/404	0/694	1/484	1/304	0/261
Sulphachloropirizadine	100	2/697	0/577	0/404	0/694	0/484	0/304	0/261
Sulphamethoxazole	100	1/697	1/577	0/404	1/694	0/484	0/304	1/261
Sulphamethazine	100	0/697	1/577	0/404	1/694	1/484	0/304	0/261
Sulphadiazine	100	0/697	0/577	0/404	1/694	0/484	2/304	1/261
Quinolones								
Ciprofloxacin/ Enrofloxacin	100	03/702	4/581	5/443	3/818	2/498; 14/498	4/307; 6/307	0/244, 14/244
Flumequine	600 in fish, 200 in crab, prawn	0/702	0/581	0/443	0/818		0/307	0/244
Difloxacin	300	00/702	0/581	0/62	0/818			
Sarafloxacin	30	0/702	0/581	0/443	0/818		0/307	0/244
Oxalonic acid	100	0/702	0/581	0/144	0/818			
Danofloxacin	100	0/702	0/581	0/62	0/818			
Florfenicol	1000	0/75	0/105	0/100	0/124		0/155	0/150
Trimethoprim	100	0/141	1/175	0/172	0/135		1/186	2/162
Neomycin							0/191	0/164
Trichlofon	ND	0/198	0/286	0/106	NT		1/300	1/266
Praziquantel	ND	NT	0/168	0/456	1/408		1/300	2/266
Trifluralin	ND	NT	22/222	9/456	3/429		1/300	0/266
Ivermectin							5/300	2/266
Malachite green/ Leucomalachite green	ND	0/364	1/289	0/255	0/232		5/264	1/246
Crystal violet/ Leucocrystal violet	ND	0/293	0/173	0/104	0/35			

1 - Number of non-compliant/Number of tested samples.

establish the minimum required performance limit for the method to be used. Most aquaculture producing countries have adopted these methods and the laboratories performing residue monitoring are accredited to ISO 17025. However, there are some antibiotics, like tetracyclines, and antiparasiticides, permitted in the EU. There is no uniformity in drugs permitted for aquaculture in many producing countries and there have been some instances of differences in MRLs and methodology used for

determining their levels. Overall, there has been a drastic reduction in import refusals and rapid alerts for veterinary drugs in aquaculture products.

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