Final Draft
চুড়ান্ত খসড়া

Guidelines for the Control of Aquaculture Medicinal Products-AMPs

অ্যাকোয়াকালচার মেডিসিনাল প্রোডাক্টস নিয়ন্ত্রণ নির্দেশিকা

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Guidelines for the Control of Aquaculture Medicinal Products–AMPs

1. Objectives and Scope

The overall objective of this Guidelines is to ensure that Aquaculture Medicinal Products (herein after reffered as Aquamedicines or AMPs) produced in or imported to Bangladesh used for the production of fish and fishery products are leading to products that are safe for consumers.

The specific objectives of the Guidelines for the control of Aquamedicines are:

- to control the use of aquamedicines across the production chain of aquaculture operations.
- to ensure that the exposure of aquatic animals to aquamedicines does not pose a risk to human health.
- to ensure that the aquaculture products produced in Bangladesh comply with the maximum residue limits (MRLs) for permitted substances.
- to prevent illegal or unauthorized use of aquamedicines.
- to monitor and verify that appropriate practices are being applied and effective measures are in place at manufacture, import, distribution, retailing, and use.

This Guidelines is intended to provide the guidance on registration, manufacture, import, distribution, retailing, and use of Aquamedicines to be followed by regulatory agencies, manufacturers, importers, wholesalers, retailers, fisheries professionals, and users.

This Guidelines may periodically undergo further refinement to comply with the current national and international requirements.

2. Legal background

This Guideline is based on the legislative framework of Bangladesh related to drugs as well as those of international guidelines pertaining to Aquaculture Medicinal Products and more specific regulations for aquaculture.

Drug related Rules of Bangladesh

- The DRUGS ACT, 1940 (XXIII OF 1940).
- The Bengal Drugs Rules, 1946 (As amended by the Government of East Bengal up to December 1952).
- The Drugs (Control) Ordinance, 1982, Ordinance No. VIII of 1982; It is an ordinance to control manufacture, import, distribution and sale of drugs.
- National Drug Policy 2005.

Fish and Fishery related Rules of Bangladesh

- Fish and Fish Products (Inspection and Quality Control) Ordinance, 1983
- Fish and Fish Products (Inspection and Quality Control) Rule 1997 (amendment 2008)
- Fish Hatchery Act 2010

- Monitoring of resistance to identify emerging health problems and planning of timely corrective actions to protect human health and.
- Guidelines for professionals to reduce overuse and misuse of antimicrobials in food animals.

3. Definitions and Abbreviations

a) Aquaculture Medicinal Products– AMPs (Aquamedicines)]	Aquaculture Medicinal Products (herein after referred to as Aquamedicines) means Medicinal Products used in aquaculture or any substance or combination of substances presented as having properties for treating or preventing disease in aquatic animals; or any substance or combination of substances which may be used in or administered to aquatic animals with a view either to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis" (Definition for VMPs in Directive 2001/82/EC). In the context of this Guidelines, the term "Aquamedicine" shall mean: "medicine and medicinal products used in aquaculture including those used in activities such as farm, hatchery and fish feed mills".
b) Aquatic animals	Aquatic animals means all life stages (including eggs and gametes) of fish, molluscs and crustaceans originating from aquaculture establishments or removed from the wild, for farming purposes, for release into the environment, for human consumption or for ornamental purposes.
c) CCC	CCC means Central Coordination Committee constituted of representatives of DGDA, Department of Fisheries and relevant experts. Director General of DGDA will decide the number of CCC members. CCC may include one of the fisheries academician as expert member from any University in its committee CCC may make recommendations related to withdrawal periods, area of use or application, target species, etc based on the relevant rules.
d) DCC	DCC means Drug Control Committee as per definition of "The Drugs (Control) Ordinance", 1982, No. 4 (f).
e) DGDA	DGDA means Directorate General of Drug Administration, whch is the Drug Regulatory and Control Agency of Bangladesh
f) DoF	DoF means Department of Fisheries of Bangladesh
g) Distribution	Distribution means transportation of goods within Bangladesh up to the retailer level

- Fish Hatchery Rules 2011
- Fish Feed and Animal Feed Act 2010
- Fish Feed Rules 2011

Codex guidelines

CODEX Code of Practice for Control of the Use of Veterinary Drugs (CAC/RCP 38-1993) laying guidelines on the prescription, application, distribution and control of drugs used for treating animals, preserving animal health or improving animal production.

OIE (Office International Epizootique–International Office for Epizootics) **guidelines**

Aquatic Animal Health Code published by OIE aiming to assure the sanitary safety of international trade in terrestrial and aquatic animals, and their products, which sets out standards for the improvement of aquatic animal health and welfare and veterinary public health worldwide, including through standards for safe international trade in aquatic animals and their products (OIE, 2011).

European Union

EU's legislation on veterinary medicines relies on three key components: 1) control of manufacture, 2) control of placing on the market, and 3) post-approval monitoring.

Key EU legal texts are as follows:

- Commission Directive 91/412/EEC laying down the principles and guidelines of good manufacturing practice for veterinary medicinal products.
- Directive 2001/82/EC on the Community code relating to veterinary medicinal products. Amended by Directive 2004/28/EC of the European Parliament
- Directive 2004/28/EC amending Directive 2001/82/EC on the Community code relating to veterinary medicinal products.
- Regulation (EC) No 726/2004 laying down Community procedures for the authorization and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency.
- Council Regulation (EEC) No 2377/90 laying down a Community procedure for the establishment of maximum residue limits for veterinary medicinal products in foodstuffs of animal origin.

Food & Agricultural Organization (FAO) Guidelines

FAO (2004: Responsible use of antibiotics in aquaculture) made recommendations designed for use by governments, veterinary and other professional societies, industry and academia. The main measures are:

- Obligatory prescriptions for all antimicrobials used for disease control.
- Creation of national systems to monitor antimicrobial usage in food animals.

h) Fisheries professionals	Fisheries professionals means graduates in fisheries or aquatic sciences, who have studied four-year university course and thus have competence to advise on prevention of aquatic animal health problems or on treatment of aquatic animal diseases (fish, molluscs, crustaceans)
i) FRCP	FRCP means Factory Residue Control Planfor control and monitoring of residues and contaminants in fish and fishery products at processing factory level.
j) Health Management Advisory note	Health Management Advisory note means an advisory note issued by fisheries professionals based on the on-farm-investigations, explaining and clarifying the nature of the disease, causative agent, treatment regime, including the dose, the treatment intervals, the duration of the treatment, the withdrawal period and the amount of Aquamedicine to be delivered, etc.
k) Labeling	Labeling means providing required information on the primary (inner) and / or secondary (outer) packaging of the product.
l) Manufacture	Manufacture means all operations including receipt of materials, processing, packaging, labeling, quality control, release, and storage of aquamedicine
m) MRL	MRL means maximum residue limits
n) NRCP	NRCP means National Residue Control Plan for control and monitoring of residues and contaminants in fish and fishery products at the primary production levels.
o) Production chain	Production chain means the series of methods or activities or stages involved in the process of production of food for human consumption.
p) Placing on the market	Placing on the market means holding of products for the purposes of sale, including offering for sale or for the purposes of any other form of transfer, whether or not free of charge, and the sale, distribution and other forms of transfer themselves.
q) Prescription	Prescription means any prescription issued by Qualified Personnel for prescription of aquamedicine.
r) Qualified Personnel	Qualified Personnel means any person who has university level formal education and knowledge in both pharmacology and aquatic animal health and disease (crustaceans, fishes and molluscs).
s) Retailing	Retailing means holding product available for sale and selling product to users.
t) Registration of Medicines	Registration of Medicines means granting of Production License and Marketing Authorization according to "The Drug (Control) Ordinance", 1982.

u) Storage	Storage means holding of aquamedicine in licensed warehouses.
v) Users	Users means all users of aquamedicines such as operators of farms, hatcheries, feed mills, nurseries.
w) Withdrawal time	Withdrawal time means the time between giving the animal its last dose of aquamedicines and the level of residues in the tissues or products falling below the Maximum Residue Limit, expressed in degree-days. Presently, the withdrawal period for all the aquatic animal species for Tetracyclines is 550 degree-days (i.e., if the mean daily water temperature during the treatment period is 25°C, then withdrawal period is 550÷25= 22 days).
x) Wholesaling	Wholesaling means any activity which includes the purchase, sale, import, export, or any other commercial transaction in aquamedicines, whether or not for profit, except for - (a) the supply by a manufacturer of aquamedicines manufactured by himself, or, (b) retail supplies of aquamedicines by persons entitled to carry out such supplies in accordance with regulation.

4. Roles and Responsibilities

The table below outlines the tasks and responsibilities of DGDA and DoF with regard to aquamedicines. Further details are outlined in the respective chapters of this Guidelines.

Responsibility / Task	ref. Chapter No.	DGDA	DoF	others
a) Granting Registration of AMPs	5.1	R		
b) Manufacturing of AMPs according to the registration and under GMP conditions	5.2			R = Pharmaceutical Manufacturers
c) Controlling Pharmaceutical Manufacturers	5.2	R		
d) Licensing and controlling of warehouses and wholesalers	5.3	R		
e) Licensing of retailers	5.3	R		
f) Controlling of retailers	5.3	R	P	
g) Keeping a register of the licensed wholesalers and retailers	5.3	R		
h) Market release of imported AMPs	5.4			R=Pharmaceutical Companies
i) Iuuse of Health Management Advisory Note for AMPs	5.5		R = Fishery Professionals	R = Qualified Personnel

Responsibility / Task	ref. Chapter No.	DGDA	DoF	others
j) Documenting the use of AMPs	5.6			R = Users (farmers)
k) Monitoring users of AMPs based on the principles of Good Aquacultural Practices	5.6		R	
l) Field Monitoring of AMPs	6		R (NRCP)	R = Processors (FRCP)
m) Implementation of the Guidelines (information and training)	7	R	R	

R = responsibility P = participation

5. Guidelines for the Control of Aquamedicines

5.1 Guideline for Obtaining Aquamedicine Registration

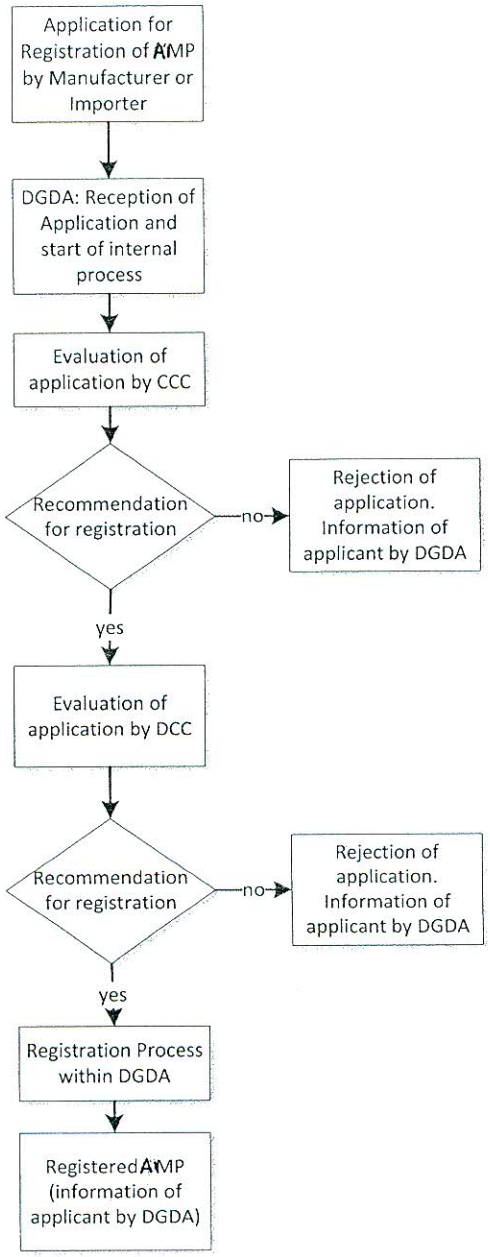
Pharmaceutical Manufacturers and Pharmaceutical Companies acting as Importers shall apply for Registration of aquamedicines. It is the authority of DGDA to assess the applications and grant Registration of aquamedicine. The registration process will be supported by committees.

In the course of this registration process, an evaluation of the application is done by the CCC. CCC may make recommendations related to withdrawal periods, area of use or application, target species, etc. The CCC may conclude that the registration shall not be granted for reasons of public health safety or aquatic animal safety. If the registration is not granted, the applicant is informed by DGDA.

If the CCC suggests registration of the aquamedicine, evaluation by the DCC is done in a subsequent step. The DCC evaluates the aquamedicine under the perspectives of e.g. actual need for the aquamedicine, environmental impact or practical aspects. If DCC decides that aquamedicine is not recommended for registration, they will inform DGDA who subsequently will inform the applicant.

If both committees suggest the registration of the aquamedicine, the internal registration process at DGDA is completed and registration of the aquamdecine is granted by DGDA. The applicant is informed by DGDA.

The work-flow of this process is outlined below.



In the course of granting the registration, DGDA shall ensure that proper labeling information and information for data sheets or leaflets, information on dosage schedules and recommended withdrawal periods are in place for the aquamedicine (The Bengal Drug Rules 1946 Article 54 and The Drug Act 1940 Chapter III 9-f).

The following information shall be shown on the product label or in the leaflet:

i. Name of the aquamedicine, its strength and active ingredients

ii. Excipients

iii. Target species

iv. Special precautions for use, including such precautions to be taken by the person administering the medicinal product
v. Dosage and administration route
vi. Withdrawal periods for the different target species
vii. Date of manufacture and expiry
viii. Batch number
ix. Storage conditions to be followed
x. for multi-dosage containers: shelf life after first opening of the container
xi. Instructions for safe disposal of non-used aquamedicine

It shall be obligatory to include a leaflet with all the required information in the packaging of aquamedicine.

5.2 Guidelines for Manufacture of Aquamedicine

Pharmaceutical Manufacturers producing aquamedicine shall follow the principles of GMP as outlined in "The Drugs (Control) Ordinance, 1982, No. 15.

The Directorate General of Drug Administration (DGDA) is responsible for control of the manufacturers to comply with these regulations.

5.3 Guidelines for Distribution, Warehousing, Wholesaling and Retailing of Aquamedicine

5.3.1 Distribution

Any distribution shall be done under the responsibility of the initiating organization, i.e. the pharmaceutical manufacturers or the importers. The initiator shall ensure that the standards of Good Distribution Practice are followed. Among these are:

- record keeping about product identity
  - product name
  - batch number
- distribution information
  - quantity
  - receiver
  - date of delivery
- temperature or other physical requirements

5.3.2 Warehousing, Wholesaling, Retailing

Licenses are required for stock keeping (warehousing), wholesaling and retailing, including the exhibit for sale of aquamedicine. Such license shall be granted by DGDA, provided that adequate premises are available and these premises are equipped with proper storage facilities for preserving the properties of the aquamedicine to which the license applies (Bengal Drug Rule (1946) Article 20 and 23).

Aquamedicine shall be stored at wholesalers and retailers in areas exclusively used for these products.

DGDA shall include wholesalers and retailers in the inspection program and keep a register of the licensed wholesalers and retailers.

Retailers shall ensure that prescription aquamedicines are provided only on producing valid Health Management Advisory Note/prescription from Fisheries Professional or Qualified Personnel. The retailers must ensure that the recipient is competent to use the product for the purpose for which it is prescribed. Only the prescribed quantity shall be sold.

The retailer shall take all precautions to avoid off-label or extra-label sale of aquamedicines.

Wholesalers and retailers will keep the following records under their custody for any transaction of aquamedicine (Bengal Drug Rule 1946 Article 24-4) for a period of two years:

i. date of supply
ii. name and address of purchaser
iii. name of the drug
iv. quantity sold
v. name of the manufacturer
vi. batch number

5.4 Guidelines for Import and Possession of Aquamedicine

No product must be imported into Bangladesh if its label or container or anything accompanying the drug bears any statement, design or device which makes any false claim for the drug (as per The Drug Act 1940 Chapter III 9 (f)).

The importer may be penalized for import of aquamedicines, if the imported aquamedicines do not have a registration /as per "The Drug (Control) Ordinance", 1982, No. 18).

All consignment of imported aquamedicines shall be accompanied by an invoice, stating generic name and list of ingredients, address of the manufacturer and quantities of the drugs (as per The Bengal Drug Rules 1946, Article: 38)

All the imported products shall comply with the registration granted by DGDA before releasing to market. Market release shall be done by Pharmaceutical manufacturers or importing Companies.

If non-registered products are found during routine inspection by the DoF, this shall be reported to DGDA for appropriate actions including seizure and destruction.

5.5 Guidelines for Issue of Advisory Note/Prescription of Aquamedicines

Aquamedicines shall only be advised by Fisheries Professionals or by Qualified Personnel, who have education and knowledge in health and disease management of aquatic animals (fishes, molluscs and crustaceans).

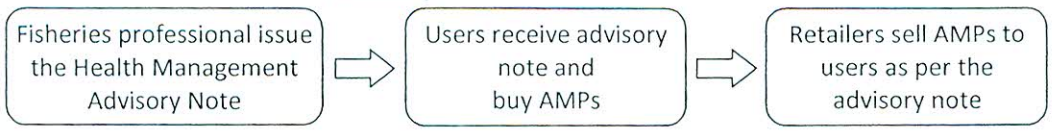
Fisheries Professional is competent and authorized to prescribe or to issue advisory note for aquamedicines, indicating precisely to the user the treatment regime, including the dose, the treatment intervals, the duration of the treatment, the withdrawal period and the quantity to be delivered depending on the dosage and the number of aquatic animals to be treated.

Currently, fisheries officers or aquatic science professionals have knowledge and experience in aquatic animal physiology, pathology, health and diseases etc but do not have education in pharmacology.

For qualified prescription of aquamedicines, both competences (knowledge in pharmacology as well as knowledge in physiology, pathology, health and diseases etc. of aquatic animals) are required. Thus, it is clear that in the current situation, there is no professional group adequately qualified to perform the prescription of aquamedicines.

The following solutions shall be followed on a immediate (short)-, medium- and long-term basis:

- **Immediate solution** - Fisheries professionals issue the Health Management Advisory note.



- **Medium-term solution** - Condensed diploma course offered for fisheries professionals on pharmacology
  - Condensed course offered through pharmacology experts
  - Command area officers will complete the above course first and get qualified; rest of the interested/existing fisheries professionals take the course and get qualified.
- **Long-term solution** - Integration of "Pharmacology" and related subjects in the curriculum of scientific education of fishery science and formation of Fisheries Council.

5.6 Guidelines for Use of Aquamedicine

The users shall make best use of preventive mechanisms such as Good Aquaculture Practice to restrict or avoid use of aquamedicines as far as possible.

The NRCP shall cover aquamedicines and their metabolites as well as heavy metals and pesticide residues. DoF shall take all necessary legal actions against non-compliance at field level residue tests.

The DoF shall publish all results annually and make trend analyses, submit the recommendations to DGDA, and also communicate such results to customs / police / border guard or other concerned control agencies as required for future course of action.

The DoF shall carry out NRCP as per the NRCP Guideline 2011 (rev. 2012).

7. Implementation of the Guidelines and Coordination of the Aquamedicine Control Program

7.1 Implementation of the Guidelines

After approval of the Guidelines by MoFL, the information and training shall be done in two phases:

- Information Phase - 2 months
- Training Phase - 2 months

The Guidelines will come in to force after completion of the aforesaid two phases.

For the implementation of theGuidelines, information and training shall be provided for the involved stakeholders:

- DGDA officials
- DoF officials
- Pharmaceutical Manufacturers / Pharmaceutical Companies as Importers
- Wholesalers
- Retailers
- Fisheries Orofessuonal or Qualified Personnel
- Users
- Processors.

The Information Phase (2 months) shall comprise the following steps:

- information among DGDA officials, which shall be done internally at DGDA by DGDA officials having been involved in the development of the Guidelines.
- information among DoF officials, which shall be done internally by officials having been involved in the development of the Guidelines.
- Pharmaceutical Manufacturers and Pharmaceutical Companies acting as importers shall be informed, followed by Fisheries Professionals, Qualified Personnel, Wholesalers, Retailers, Users and Processors. The information of the involved stakeholders shall be done by DGDA or DoF.

During the Information Phase, a detailed program for the 2-months Training Phase shall be elaborated jointly by DGDA and DoF (with support from advisors or consultants as feasible) and training on the specific elements of the Guidelines shall be

performed in this phase by DGDA and DoF. The authorities may appoint consultants or advisors to perform such training.

7.2 Co-ordination of the Aquamedicine Control Program

DoF of the Ministry of Fisheries and Livestock operates the aquamedicine control program with the coordination from DGDA, meeting the following requirements:

- This Guidelines is based on the national legislation governing the registration, manufacture, distribution, wholesaling, retailing and the use of aquamedicines
- DoF and DGDA have sufficient financial resources to carry out the control program as planned.

8. Validity of the Guidelines

This Guidelines is for controlling aquamedicine to ensure production of safe aquatic food products for both, domestic and international markets and is based on existing legal structures.

A continuous monitoring of the implementation processes of this Guidelines shall be performed. Based on the results of such evaluation, the need for adaptation or modification of this Guidelines or the development of further legal framework shall be considered.