Existing AMR surveillance programme/network in fisheries sector in India and suggestions for future framework

Prof. T.J. Abraham
Department of Aquatic Animal Health
Faculty of Fishery Sciences
WB University of Animal and Fishery Sciences,
Chakgaria, Kolkata – 700094, West Bengal, India
Indian Aquaculture

- **Finfish culture**
  - Freshwater: Carps, catfish, tilapia, many ornamental fish
  - Saltwater: Mullet, sea bass, etc

- **Shellfish culture**
  - Freshwater: *Macrobrachium* spp.
  - Saltwater: *Penaeus* spp.

Culture systems

- Natural water bodies
- Dug-out Ponds
- Extensive
- Modified extensive
- Semi-intensive
- Intensive
- Flow-through systems
- Recirculating systems (Rarely)
Fish may be raised/farmed for
- Human consumption (e.g. carps, catfish, tilapia)
- Restoring native populations in the wild (Ranging)
- Stocking for fishing (culture based capture fishery)
- Bait and Aquariums/hobby

### Major freshwater fish species cultured in India

<table>
<thead>
<tr>
<th>Major and minor carps</th>
<th>Exotic carps</th>
<th>Catfish</th>
<th>Other species</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Catla catla, Labeo rohita, Cirrhinus mrigala L. bata, L. calbasu, Puntius javanicus Puntius spp., etc</strong></td>
<td><strong>Cyprinus carpio, Ctenopharyngodon idella, Hypophthalmichthys molitrix, Aristichthys nobilis, Mylopharyngodon piceus, etc</strong></td>
<td><strong>Clarias batrachus, C. gariepinus, C. macrocephalus Heteropneustes fossilis, P. pangasius, Pangasius sutchi, Pangasinodon hypophthalmus, Ompak pabda, Sperata gulio S. tangra, etc</strong></td>
<td><strong>Oreochromis mossambicus, O. niloticus, Anabas testudineus, Chitala chitala Channa spp., Piaractus brachypomus, Ornamental fish species</strong></td>
</tr>
</tbody>
</table>

6/26/2018
Diseases in Aquaculture

- Carps
- Catfish
- Tilapia
- Salmonids
- Shrimp
- Abalone
- Oysters
Why are diseases important to aquaculture?

- 1971: *Flexibacter columnaris*, a bacterium, kills 14 million wild fish in Klamath Lake

- Developing countries in Asia lost at least US$1400 million due to diseases in 1990 alone.

- World Bank report: global losses due to shrimp disease are around US$ 3 thousand million

- In 2010, aquaculture in China suffered production losses of *worth US$ 3.3 billion* caused by diseases, natural disasters, pollution, etc.

- Global Aquaculture Alliance world survey estimated at about *22% disease loss in 2001*

- Total loss for the past 15 years probably in excess of $15 billion
Available estimates of economic losses due to EUS

<table>
<thead>
<tr>
<th>Country</th>
<th>Year</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thailand</td>
<td>1983-1993</td>
<td>US$ 100 M</td>
</tr>
<tr>
<td>Bangladesh</td>
<td>1988-1989</td>
<td>US$ 4.8 M</td>
</tr>
<tr>
<td>Indonesia</td>
<td>1980-1987</td>
<td>US$ 235 000</td>
</tr>
<tr>
<td>Pakistan</td>
<td>1996</td>
<td>US$ 300 000</td>
</tr>
<tr>
<td>Eastern Australia</td>
<td>Annually</td>
<td>US$ 700 000</td>
</tr>
<tr>
<td>India (Bihar, Orissa and Kerala)</td>
<td>1989-1992</td>
<td><strong>US$ 870,000</strong></td>
</tr>
<tr>
<td>Sri Lanka</td>
<td>Up to 1993</td>
<td>US$ 800,000</td>
</tr>
</tbody>
</table>

Losses of US$ 1.0 million due to disease-induced mortality and impaired growth are incurred annually in Andhra Pradesh.

The total losses due to argulosis in Indian carp culture have been estimated as Rs. 29,524.40/ha/year.
Finfish diseases (n=459)

- Bacterial: 1.31%
- Fungal: 0.44%
- Viral: 5.66%
- Parasitic: 3.49%
- Genetic disorder: 16.12%
- Nutritional: 1.53%
- Vertebral deformity: 62.31%
- Skeletal deformity: 2.83%
- Neoplasia: 1.96%
- Environmental: 2.61%
- Normal: 0.44%

6/26/2018
# Disease management

- **Antibiotics:**
  - Used in aquaculture ponds to control disease.
  - Antibiotics enter the water column and are ingested by wild aquatic life
  - Drug residues exceeded safe levels in wild fish around aquaculture nets.
  - Antibiotic usage raises the risk of bacteria becoming MDR

- The **Unregulated/ unapproved drugs** administered to aquacultured fish pose a potential human health hazard

- These substances may be carcinogenic, allergenic, and/or may cause antibiotic resistance in man
Table 1. Number of drugs approved for aquaculture in the world (adapted from: Schnick et al., 1997 and Daniel, 2002*).

<table>
<thead>
<tr>
<th>Drug type</th>
<th>Australia</th>
<th>Canada</th>
<th>Europe*</th>
<th>Japan</th>
<th>USA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antimicrobials</td>
<td>--</td>
<td>4</td>
<td>7†</td>
<td>27</td>
<td>3</td>
</tr>
<tr>
<td>Microbicides</td>
<td>--</td>
<td>4</td>
<td>6‡‡</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Anaesthetics</td>
<td>1</td>
<td>2</td>
<td>1+++</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Hormones</td>
<td>3</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
</tbody>
</table>

†Amoxicillin, florfenicol, flumequine, oxolinic acid, oxytetracycline, sarafloxacin and sulfadiazine-trimethoprim.
‡‡Azamethiphos, bronopol, cypermethrin, emamectin benzoate, hydrogen peroxide and teflubenzuron.
+++Tricaine methane sulphonate (MS222).

Table 2. Types of antimicrobial agents, target use and application method (adapted from Goldburg et al., 2001).

<table>
<thead>
<tr>
<th>Type of agent</th>
<th>Usage</th>
<th>Method of application</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemotherapeutants</td>
<td>Treatment of bacterial fish diseases</td>
<td>Oral – medicated feed; injection; topical; bath</td>
</tr>
<tr>
<td>Parasiticides</td>
<td>Control of sea lice on salmon; treatment of parasites in ornamental fish ponds; control of protozoa and trematodes on finfish</td>
<td>Oral – medicated feed; bath; dip; flush</td>
</tr>
<tr>
<td>Oxidants</td>
<td>To kill disease organisms and phytoplankton in pond systems</td>
<td>Direct; flush</td>
</tr>
<tr>
<td>Biocides, algicides and herbicides</td>
<td>Reduce plant growth in pond systems; antifouling treatment for fish farm cage netting</td>
<td>Direct; flush</td>
</tr>
</tbody>
</table>
Approved Drugs for Use in Aquaculture

Immersion

Formalin
- Formalin-F™ - NADA 137-687 | FOI Summary |
- Formamide-B - ANADA 200-414
- Paracide-F® - NADA 140-831 | FOI Summary |
- Parasite-S® - NADA 140-989 | FOI Summary |

Hydrogen peroxide
- 35% PEROX-AID® - NADA 141-255 | FOI Summary |
- EA |
- FONSI |

Oxytetracycline hydrochloride
- Oxymarine™ - NADA 130-435 | FOI Summary |
- Oxytetracycline HCl Soluble Powder-343 - ANADA 200-247 | FOI Summary |
- TERRAMYCIN 343 (oxytetracycline HCl) Soluble Powder - NADA 008-622 | FOI Summary |
- TETROXY Aquatic - ANADA 200-460 | FOI Summary |

Tricaine methanesulfonate
- Finquel® - NADA 042-427
In India:

Approval on quadrugs or approved quadrugs list: Nil

COASTAL AQUACULTURE AUTHORITY
Ministry of Agriculture and Farmers Welfare
Government of India
12A, Bharathi Street, G.D.R. Tower, Vanuvampettai
Madipakkam Post, Chennai – 600 091

APPLICATION FOR REGISTERING ANTIBIOTIC FREE AQUACULTURE INPUTS

1. Name of the applicant(s)/ registered company/ establishment (in BLOCK LETTERS with permanent address)

Coastal Aquaculture Authority
Government of India
Ministry of Agriculture and Farmers’ Welfare

NOTICE TO SHRIMP HATCHERY OPERATORS AND FARMERS

Shrimp hatchery operators and farmers are to use only the Registered Antibiotic-free Aquaculture Inputs in their hatchery and Farms.

LIST OF REGISTERED ANTIBIOTIC-FREE AQUACULTURE INPUTS

<table>
<thead>
<tr>
<th>REGN. No.</th>
<th>PRODUCT</th>
<th>MANUFACTURER / DISTRIBUTOR</th>
<th>REGN. DATE</th>
<th>VALID UP TO</th>
</tr>
</thead>
</table>
MPEDA - Residue Control activities:

- Testing of samples under NRCP. (LC-MS-MS)
- Pre-harvest testing of Aquaculture produce (by ELISA/LC-MS-MS)
- Awareness campaigns in farming areas in all the maritime states
- Monitoring of farming activities and hatchery operations
Current status of AMR surveillance

Laboratory-based surveillance (LBS)

- Laboratory-based data without linkage to farm/pond/species information is frequently used to study the AMR.

- **No regular monitoring**

- LBS approach does not provide information on the extent of the problem in the population and is not promoted in GLASS.
Clinical and Laboratory Standards Institute

Aquaculture Guidelines for In-vitro Antibiotic Susceptibility Testing

- Disk diffusion testing
- MIC testing
- Interpreting test results
Global surveillance programmes that monitor resistance in specific bacterial pathogens, such as *Mycobacterium tuberculosis* and *Neisseria gonorrhoeae*, have been in place for many years.

International standards on AMR surveillance and monitoring programmes exist for some aspects of animal health.

Standards across the medical, veterinary, agricultural and environmental sectors are not harmonized, except for food-borne and zoonotic bacteria.
Priority specimens and pathogens for surveillance of AMR

- **Human Samples:** Blood, urine, faeces, Urethral and cervical swabs

- WHO list: Critical priority (3), high priority (6) and medium priority (3)

### WHO PRIORITY PATHOGENS LIST FOR R&D OF NEW ANTIBIOTICS

#### Priority 1: CRITICAL

- *Acinetobacter baumannii*, carbapenem-resistant
- *Pseudomonas aeruginosa*, carbapenem-resistant
- *Enterobacteriaceae**, carbapenem-resistant, 3rd generation cephalosporin-resistant

#### Priority 2: HIGH

- *Enterococcus faecium*, vancomycin-resistant
- *Staphylococcus aureus*, methicillin-resistant, vancomycin intermediate and resistant
- *Helicobacter pylori*, clarithromycin-resistant
- *Campylobacter*, fluoroquinolone-resistant
- *Salmonella spp.*, fluoroquinolone-resistant
- *Neisseria gonorrhoeae*, 3rd generation cephalosporin-resistant, fluoroquinolone-resistant

#### Priority 3: MEDIUM

- *Streptococcus pneumoniae*, penicillin-non-susceptible
- *Haemophilus influenzae*, ampicillin-resistant
- *Shigella spp.*, fluoroquinolone-resistant
Target bacteria

- Food-borne bacteria:
  - *Salmonella, Campylobacter*
  - *E. coli, Enterococcus* spp.
- Other bacteria: *Staphylococcus, Clostridium*

- Fish-borne bacteria: Nil
- Those associated with aquaculture:
  - Marine fish: *Vibrio* spp.
  - Freshwater fish: ????

Elements of a programme of Integrated surveillance of AMR in fish-borne bacteria

- The programme should contain the elements as outlined in Integrated surveillance of AMR in foodborne bacteria: Application of a one health approach (WHO, 2017)
Priority specimens and pathogens for surveillance of AMR for fish: Nil

- Austin and Austin (2012) Listed >110 bacterial pathogens of fish
- Level of containment: Not clear
- Ranking of pathogens: Nil

- **CLSI - Ongoing Research:** Standardizing methods and criteria for interpreting test results for fastidious bacterial pathogens of fish including:
  - *Flavobacterium columnare/psychrophilum*
  - *Streptococcus* spp. (including *S. phocae*)
  - *Vibrio* spp.
**Bacterial pathogens transmissible to human beings through contact with fish living in the wild and fish in aquacultures**

- *Mycobacterium* spp.  
- *Photobacterium damselae*  
- *Vibrio vulnificus*  
- *Streptococcus iniae*  
- *Vibrio alginolyticus*  
- *Erysipelothrix rhusiopathiae*  

**Foodborne pathogens associated with fish and fish products**

- *Vibrio parahaemolyticus* and other vibrios  
- *Escherichia coli*  
- *Salmonella* spp.  
- *Listeria monocytogenes*  
- *Clostridium perfringens*  
- *Vibrio cholerae*  
- *Aeromonas* spp.  
- *Staphylococcus aureus*  
- *Clostridium botulinum*  
- *Campylobacter jejuni* (rare)  

**Other significant bacterial species**

- *Delftia acidovorans*  
- *Legionella pneumophila*  
- *Shigella* spp.  
- *Edwardsiella tarda*  
- *Plesiomonas shigelloides*
Human bacterial pathogens indigenous to fish

Clostridium botulinum
V. cholerae
Other Vibrio spp.
A. hydrophila
Plesiromonas shigelloides

Vibrio parahaemolyticus
V. vulnificus,
Listeria monocytogenes
Other Aeromonas spp.

Pathogen–antimicrobial combinations on which GLASS will gather data: Nil

Antibiotics:
Oxytetracycline/ tetracycline,
Sulfadimethoxine and Ormetoprim,
Florfenicol**
Enrofloxacin*

6/26/2018
Antibiotic use in India

- In 2010, India was the world’s largest consumer of antibiotics for human health at 12.9 x 10^9 units (10.7 units per person).

- The next largest consumers were China at 10.0 x 10^9 units and the US at 6.8 x 10^9 units (22.0 units per person).

- 76% of the overall increase in global antibiotic consumption between 2000 and 2010 was attributable to BRICS countries, i.e., Brazil, Russia, India, China, and South Africa.

- Ampicillin and co-trimoxazole use is declining in India, while quinolone consumption is high and increasing in India.

- The scale-up in antibiotic use in India has been enabled by rapid economic growth and rising incomes, which have not translated into improvements in water, sanitation, and public health
This network will focus on
(i) diarrhea (e.g., *Shigella, Vibrio cholerae*),
(ii) enteric fever (e.g., *Salmonella Typhi, S. Paratyphi*),
(iii) sepsis caused by Enterobacteriaceae (e.g., *E. coli, Klebsiella pneumoniae*),
(iv) other Gram-negative organisms (e.g., *Pseudomonas aeruginosa, Acinetobacter baumannii*),
(v) Gram-positive bacteria (e.g., *MRSA and vancomycin-resistant enterococci [VRE]*),
(vi) fungal infections (e.g., *Candida spp.*), and
(vii) respiratory pathogens (e.g., *Streptococcus pneumoniae*).

The **ICMR has established a National Programme on AMR surveillance** in ten laboratories based at academic centers and covering priority pathogens identified by the World Health Organization.
ICAR: All India Network Project on FISH HEALTH: (July 2015-March 2020) – 10 centers

Thematic area I:
Aquaculture medicines and therapeutics

- Classification and categorisation of aquaculture drugs/ chemicals and setting standards
  - Questionnaire based collection of information on the medicines/drugs and testing kits used in aquaculture

- Addressing the food safety concerns of aquaculture drugs
  - Evaluation of efficiency (dose and schedule) of active ingredients
  - Determination of biosafety of OTC and withdrawal period
  - Residues in aquaculture sediments and water

- Drug: OTC against *Aeromonas hydrophila* and *A. caviae* infection in tilapia
Thematic area II: Strategies for disease prevention including biosecurity and quarantine

- Popularizing biosecurity protocols and BMPs
  - Awareness programs/meetings on BMPs in aquaculture
  - Training programs for stakeholders on principles and practice of BMPs
  - Advisories to stakeholders in regional languages

Thematic area III: Economic loss assessment of aquatic animal diseases

Assessment of economic impact of major aquaculture diseases

National Surveillance Programme on Aquatic Animal Diseases:
2013-2018: 32 centers
### Prevalence of Diseases/Abnormalities in Freshwater Food Fish

<table>
<thead>
<tr>
<th>Condition</th>
<th>Cause</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aeromoniasis</td>
<td><em>Ergasilus</em> infestation</td>
<td>Mixed bacterial infection</td>
</tr>
<tr>
<td>Anoxia</td>
<td>Flavobacteriosis</td>
<td>Mixed parasitic infection</td>
</tr>
<tr>
<td>Argulosis</td>
<td><em>Flectobacillus</em></td>
<td>Myxoboliasis</td>
</tr>
<tr>
<td><strong>Bacillus infection</strong></td>
<td>Eye disease</td>
<td>Nematode infestation</td>
</tr>
<tr>
<td>Bacterial gill disease</td>
<td>Fin and tail rot</td>
<td>Nutritional deficiency</td>
</tr>
<tr>
<td>Black gill disease</td>
<td>Fish opercula deformity syndrome</td>
<td>Pacu fry mortality syndrome</td>
</tr>
<tr>
<td>Cauliflower disease</td>
<td>Genetic disorder</td>
<td>Pancreatitis</td>
</tr>
<tr>
<td><strong>Citrobacter freundii infection</strong></td>
<td>Gill disease/rot/necrosis</td>
<td>Pseudomonias</td>
</tr>
<tr>
<td><em>Chilodonella</em> infestation</td>
<td>Gyrodactylosis</td>
<td>Ruptured intestine syndrome</td>
</tr>
<tr>
<td><strong>Chryseobacterium infection</strong></td>
<td>Haemorrhagic blister</td>
<td>Scoliosis</td>
</tr>
<tr>
<td>Columnaris</td>
<td>Haemorrhagic septicaemia</td>
<td>Skeletal deformity</td>
</tr>
<tr>
<td><strong>Corynebacterium infection</strong></td>
<td>Hepatitis</td>
<td>Spinning disease</td>
</tr>
<tr>
<td>Cutaneous haemorrhage</td>
<td>Ich disease</td>
<td><em>Stenotrophomonas maltophilia</em> infection</td>
</tr>
<tr>
<td><strong>Dactylogyrus infestation</strong></td>
<td><em>Ichthyoboda</em> infestation</td>
<td>Streptococcosis</td>
</tr>
<tr>
<td>Dermatitis</td>
<td>Kidney myxobolias</td>
<td>Thelohanellosis</td>
</tr>
<tr>
<td>Dropsy</td>
<td>Lactobacillos</td>
<td>Trematode infestation</td>
</tr>
<tr>
<td>Edwardsiellosis</td>
<td>Leech infestation</td>
<td>Trichodina infestation</td>
</tr>
<tr>
<td>Egg disease</td>
<td>Larnaeasis</td>
<td>Tumour / Neoplasia</td>
</tr>
<tr>
<td>Enterobacteriaceae infection</td>
<td>Lordosis</td>
<td>Ulcer</td>
</tr>
<tr>
<td>Epizootic ulcerative syndrome</td>
<td>Microcystis intoxication</td>
<td></td>
</tr>
</tbody>
</table>
Antibiotic susceptibility of bacterial strains (n=45/66) from diseased tilapia and shrimp

<table>
<thead>
<tr>
<th>Antibiotics, µg/disc</th>
<th>Tilapia: Number of strains [Motile aeromonads] (n=45)</th>
<th>Shrimp: Number of strains [Vibrios] (n=66)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Susceptible</td>
<td>Resistant</td>
</tr>
<tr>
<td>Amoxyclov, 30</td>
<td>9</td>
<td>36</td>
</tr>
<tr>
<td>Chloramphenicol, 30</td>
<td>34</td>
<td>11</td>
</tr>
<tr>
<td>Ciprofloxacin, 5</td>
<td>15</td>
<td>30</td>
</tr>
<tr>
<td>Clindamycin, 2</td>
<td>2</td>
<td>43</td>
</tr>
<tr>
<td>Co-trimoxazole, 25</td>
<td>28</td>
<td>17</td>
</tr>
<tr>
<td>Erythromycin, 15</td>
<td>0</td>
<td>45</td>
</tr>
<tr>
<td>Gatifloxacin, 5</td>
<td>29</td>
<td>16</td>
</tr>
<tr>
<td>Gentamycin, 10</td>
<td>14</td>
<td>31</td>
</tr>
<tr>
<td>Nitrofurantoin, 300</td>
<td>12</td>
<td>33</td>
</tr>
<tr>
<td>Oxytetracycline, 30</td>
<td>32</td>
<td>13</td>
</tr>
<tr>
<td>Sulphafurazole, 300</td>
<td>36</td>
<td>9</td>
</tr>
<tr>
<td>Vancomycin, 30</td>
<td>0</td>
<td>45</td>
</tr>
</tbody>
</table>
Antimicrobial use and salmon/trout production, Norway, after introduction of vaccination, 1994

Figure 4. Total sales, in tonnes of active substance, of antimicrobial veterinary medicinal products (VMPs) for therapeutic use in farmed fish in Norway in the period 1981-2014 versus produced biomass (slaughtered) farmed fish.

Figure 5A. Milligram antibacterial agents used per kilo fish produced during 1981-1993.

Antibiotics usage in Chilean salmon farms during 2015 = 660 g/ton salmon produced
Thank you 😊