Aquaculture health, AMU and AMR, and status of AMR National Action Plan in China

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Contents

◆ Brief introduction of Aquaculture in China
◆ Major bacterial pathogens and national control programme
◆ AMU in aquaculture
◆ Antibiotic Residue Monitoring Programme
◆ National Action Plans for AMR control in China
◆ Some results of AMR survey
AMU and AMR in aquaculture are related to geographical region, unit yield, fish value, culture style, type of water body, fish species, major type of bacterial disease, and type of antibacterial agent commonly used.
Trends in aquaculture production in China, 1991-2014
Major mariculture aquaculture producers by province
Major freshwater aquaculture producers by province
Relative changes of aquaculture production and area (unit yield) in 2013-2014

- Inland aquaculture (overall)
- Fish
- Crustaceans

Increasing extent (%)

- Yield
- Culture area
Freshwater aqua-production by fish species (2014)
Mariculture production by fish species (2014)

- Fish
- Shrimp
- Crab

Tonnes: 0, 200000, 400000, 600000, 800000, 1000000, 1200000

Species: Grouper, Sea bass, Turbot, Flounder, Large yellow croaker, Cobia, Seriola, Red drum, Sea bream, Puffer fish, Pacific white shrimp, Giant tiger prawn, Kuruma shrimp, Chinese white shrimp, Crab.
Top five fish species and three crustaceans cultured in China

Inland aquaculture (excluding various kinds of carp):
- Tilapia (*Oreochromis* spp.)
- Snakehead (*Channa argus*)
- largemouth catfish (*Silurus meridionalis* Chen)
- Rice field eel (*Monopterus albus*)
- largemouth bass (*Micropterus salmoides*)

Chinese mitten crab (*Eriocheir sinensis*)
- Pacific white shrimp (*Litopenaeus vannamei*)
- Red swamp crayfish (*Procambarus clarkii*)
Mariculture

Large yellow croaker (Larimichthys crocea)
Turbot (Scophthalmus maximus)
Sea bass (Lateolabrax japonicus)
Grouper fish (Epinephelus spp.)
Red drum (Sciaenops ocellatus)

Pacific white shrimp (Litopenaeus vannamei)
Swimming crab (Portunus trituberculatus)
mud crab (Scylla paramamosain)
Giant tiger prawn (Penaeus monodon)
Chinese white shrimp (Fenneropenaeus chinensis)
Freshwater aqua-production by water bodies

- Pond: 72%
- Lake: 5%
- Reservoir: 13%
- Streams: 3%
- Paddy field: 5%
- Others: 2%
# List of pathogenic Gram-negative bacteria in China

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Disease</th>
<th>Host of pathogen</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Aeromonas hydrophila</em></td>
<td>Motile aeromonads septicemia (MAS)</td>
<td>Catfish, carp, trout, eel, sturgeon, tilapia and bass, etc.</td>
</tr>
<tr>
<td><em>Aeromonas salmonicida</em></td>
<td>Furunculosis</td>
<td>Salmon, trout, carp and catfish</td>
</tr>
<tr>
<td>Other <em>Aeromonas</em> species</td>
<td>MAS</td>
<td>Carp, catfish, eel, sturgeon, tilapia, etc.</td>
</tr>
<tr>
<td><em>Edwardsiella ictaluri</em></td>
<td>Enteric septicaemia of catfish</td>
<td>Catfish, yellow catfish</td>
</tr>
<tr>
<td><em>Edwardsiella tarda</em></td>
<td>Edwardsiellosis or putrefactive disease</td>
<td>Turbot, flounder, carp, catfish, eel and tilapia</td>
</tr>
<tr>
<td><em>Flavobacterium columnare</em></td>
<td>Columnaris</td>
<td>Carp, mandarin fish, trout, tilapia, catfish and salmon</td>
</tr>
<tr>
<td><em>Flavobacterium psychrophilum</em></td>
<td>Flavobacteriosis</td>
<td>Trout</td>
</tr>
<tr>
<td><em>Citrobacter spp.</em></td>
<td>Pasteurellosis</td>
<td>Carp, sturgeon, crab, crayfish, softshell turtle, sturgeons</td>
</tr>
<tr>
<td><em>Acinetobacter spp.</em></td>
<td></td>
<td>Sturgeon, sea bream, yellow catfish, sea bass, snakehead</td>
</tr>
<tr>
<td><em>Photobacterium spp.</em></td>
<td>Pseudomonads septicemia</td>
<td>Carp, catfish, eel, salmon</td>
</tr>
<tr>
<td><em>Pseudomonas spp.</em></td>
<td></td>
<td>Most of the marine fish species, crayfish</td>
</tr>
<tr>
<td><em>Vibrio spp.</em></td>
<td>Pasturellosis</td>
<td>Trout</td>
</tr>
<tr>
<td><em>Yersinia ruckeri</em></td>
<td>Yersiniosis or enteric red mouth disease</td>
<td>Trout and salmon</td>
</tr>
</tbody>
</table>
## List of pathogenic Gram-positive bacteria reported in China

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Disease</th>
<th>Host of pathogen</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Lactococcus garvieae</em></td>
<td>Lactococcosis</td>
<td>flounder, soft-shell turtle, crayfish</td>
</tr>
<tr>
<td><em>Nocardia</em> sp.</td>
<td>Nocardiosis</td>
<td>Snakehead, large yellow croakers, seriola, largemouth bass, <em>Trachinotus ovatus</em></td>
</tr>
<tr>
<td><em>Streptococcus agalactiae</em></td>
<td>Streptococcosis</td>
<td>Tilapia, Grouper</td>
</tr>
<tr>
<td><em>Streptococcus iniae</em></td>
<td>Streptococcosis</td>
<td>Tilapia, sea bream, flounder, hybrid striped bass</td>
</tr>
<tr>
<td><em>Streptococcus dysgalactiae</em></td>
<td>Streptococcosis</td>
<td>Sturgeon</td>
</tr>
<tr>
<td><em>Weissella</em> sp.</td>
<td>Haemorrhagic septicaemia</td>
<td>Trout</td>
</tr>
<tr>
<td>Mycobacterium spp.</td>
<td>Fish tuberculosis</td>
<td>sturgeon</td>
</tr>
</tbody>
</table>
Total economic loss resulting from diseases of farmed aquatic animals only in the year of 2015:

- 13.2 billion RMB yuan≈1.9 billion US$,
- accounting for 1.6% of total output value from aquaculture
- Fish drug industry output value was ≈1.5 billion RMB yuan
Distribution of economic loss caused by diseases by group of species in 2015

- Crustaceans, 52%
- Fish, 32%
- Shellfish, 11%
- Others, 5%
Characteristics of occurrence of farmed aquatic animal diseases in China in 2015

- The number of diseased farmed species, and the number of category of diseases maintain high level.
- Risk of important plagues are still high.
- Shrimp is the cultured species with highest economic loss caused by varieties of diseases, and grass carp is the fish species suffering the greatest economic loss.
- There are frequent regional disease outbreaks.
- Highest incidence seasons of fish diseases are from April to June, and from August to September.
Analysis of the causes of farmed aquatic animals diseases

- Pollution of aquaculture water is difficult to control
- Healthy farming mode and technology is difficult to implement
- Drugs are not administrated scientifically
- Quality of fish seed is not stable
- There are several kinds of disease which have no effective drugs so far.
China's Aquatic Animal Epidemic Prevention System

◆ The regional aquatic animal epidemic prevention technology laboratories:
◆ 13 provincial aquatic animal disease control center,
◆ 628 county aquatic animal disease prevention station.
◆ Remote diagnosis system for aquatic animal diseases.
◆ Epidemic monitoring system (network) consisting of more 4210 monitoring and reporting spots.
36 kinds of major diseases (7 of them are bacterial disease) are routinely monitored and reported around the year.

Eight high-risk virus are the main targets for monitoring:

• Spring viraemia of carp virus (SVCV) in carp
• White spot syndrome virus (WSSV) in shrimp and crab
• Viral nervous necrosis virus (VNNV) in marine fish
• Infectious haematopoietic necrosis virus (IHNV) in salmonids
• Koi herpes virus (KHV) in Koi and carp
• Hematopoietic Necrosis caused by Cyprinid Herpesvirus 2 (CyHV-2) in Carassius auratus gibelio
• Grass carp hemorrhage caused by grass carp reovirus (GCRV)
• Infectious hypodermal and hematopoietic necrosis (IHHN) in shrimp

National List of Aquatic Pathogens that is subject of monitoring and control programme
<table>
<thead>
<tr>
<th><strong>Antimicrobial agents allowed to use in aquaculture</strong></th>
<th><strong>Antimicrobial agents not allowed to use in aquaculture</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Neomycin Sulphate</td>
<td>Norfloxacin</td>
</tr>
<tr>
<td>Doxycycline Hydrochloride</td>
<td>Ciprofloxacin</td>
</tr>
<tr>
<td>Thiamphenicol</td>
<td>Erythromycin</td>
</tr>
<tr>
<td>flofenicol</td>
<td>chloramphenicol</td>
</tr>
<tr>
<td>Sulfadiazine(SD) ,</td>
<td>Tylosin</td>
</tr>
<tr>
<td>Sulfamethoxazole(SMZ)/TMP ,</td>
<td>Bacitracin Zinc</td>
</tr>
<tr>
<td>Sulfadimidine(SM2) , Sodium</td>
<td>Nitrofurans (Furazolldone,</td>
</tr>
<tr>
<td>sulfamonomethoxine (SMM-Na)</td>
<td>Nitrofurazon, Nitrofurantoin, etc)</td>
</tr>
<tr>
<td>Enrofloxacin</td>
<td>Olaquindox</td>
</tr>
<tr>
<td>Flumequine</td>
<td></td>
</tr>
<tr>
<td>Oxolinic Acid</td>
<td></td>
</tr>
<tr>
<td>oxytetracycline</td>
<td></td>
</tr>
</tbody>
</table>
## Approved fish vaccines in China

<table>
<thead>
<tr>
<th>Pathogens or vaccines</th>
<th>Target host or diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Edwardsiella tarda</em> (strain EIBAV1) avirulent live vaccine</td>
<td><em>Scophthalmus maximus</em> (Turbot)</td>
</tr>
<tr>
<td><em>Aeromonas hydrophila</em> (strain J1)</td>
<td>Motile Aeromonads Septicemia (MAS) of freshwater fish</td>
</tr>
<tr>
<td>Grass carp reovirus, GCRV (Killed)</td>
<td><em>Ctenopharyngodon idellus</em> (Grass carp) &amp; Mylopharyngodon piceus (black carp)</td>
</tr>
<tr>
<td>Grass carp reovirus, GCRV (Attenuated)</td>
<td></td>
</tr>
<tr>
<td>Inactivated Diseased fish Tissue homogenate vaccine</td>
<td></td>
</tr>
<tr>
<td>Multi-vaccine of anti-idiotypic antibody against <em>Vibrio alginolyticus</em>, <em>Vibrio</em></td>
<td><em>Paralichthys olivaceus</em> (Flounder)</td>
</tr>
<tr>
<td><em>anguillarum</em> and <em>Edwardsiella tarda</em></td>
<td></td>
</tr>
<tr>
<td>Iridovirus (strain Ehime-1 and GF14)</td>
<td><em>Pagrus major, Seriola</em> spp., <em>Pseudocaranx dentex</em></td>
</tr>
<tr>
<td><em>Lactococcus garvieae</em> (strain BY1)</td>
<td><em>Seriola quinqueradiata</em></td>
</tr>
</tbody>
</table>

Approved fish vaccines in China
REGULATIONS ON ADMINISTRATION OF VETERINARY DRUGS
effective from 2014

◆ The Registration, Manufacture, Distribution, Import and Export, use, Supervision and Administration of veterinary drugs and vaccines (including those used in aquaculture) must comply with this law.

◆ Veterinary Bureau, Ministry of Agriculture and its provincial branches are responsible for enforcing the law.
For more than 10 years there are no new antimicrobial chemicals (except herbal medicine) have been developed for use in aquaculture because of restrict registration requirement and high development costs.
To implement the "Agricultural product quality and safety law", "food safety law", to comprehensive grasp the quality and safety of agricultural products in China, and to strengthen the agricultural product quality and safety supervision, Ministry of Agriculture has carried out a routine monitoring program of national agricultural product quality (including aquatic products) (safety risk monitoring) from 2001.

Department of Technology and Quality Supervision (DTQS), Fisheries Bureau, Ministry of Agriculture, is responsible for the organization and implementation of the programme.
The monitoring focused on chloramphenicol, malachite green, Nitrofurans, sulfonamides, quinolones in the following aquatic animals on market: Tilapia, large yellow croaker, turbot, largemouth bass, grass carp, common carp, crucian carp, crayfish, crab, silver carp, bighead carp, snakehead fish, bream, and mandarin fish.

Have established a large and perfect monitoring and testing system. Qualified agricultural product quality and safety testing organization cross the country undertake routine monitoring works.

Ministry of Agriculture issues regular monitoring statistic information of quality and safety of agricultural products quarterly.

Published on August 5, 2016

Action plan at National level

国立健康和社会保障部

关于印发《遏制细菌性药物国家行动计划（2016-2020年）的通知

卫发（2016）43号

各省、自治区、直辖市及新疆生产建设兵团卫生计生委（卫生局）、发展改革委、教育部（教委、教
育局）、科技部（委）、工业和信息化部（信息经济司）、环保厅（局）、国土资源部（局）、环境保护
厅（局）、农业部（农委、农村经济、畜牧兽医局）厅（委、局）、文化厅（局）、新闻出版广电局、食
品药品监督管理局，中医药管理局，解放军各大单位卫生部门：

为积极应对细菌耐药带来的挑战，提高抗菌药物科学管理水平，遏制细菌药物发展与蔓延，维护
人民群众身体健康，促进经济社会发展，国家卫生计生委等14部门联合制定了《遏制细菌性药物国
家行动计划（2016-2020年）》（以下简称《行动计划》）。现印发你们，请结合实际，各部门的工作实际组织实
施，切实落实各项政策和保障措施，保证《行动计划》目标如期实现。

国家卫生计生委 国家发展改革委
教育部 科技部
工业和信息化部 财政部
环境保护部 国土资源部
农业部 文化部
新闻出版广电局 食品药品监督管理局
中医药管理局 中央军委后勤保障部

2016年8月5日
The Goals of the National Action Plan
Concerning AMU and AMR in veterinary sector (including aquaculture)

✓ The proportion of sales with veterinary prescription of antibacterial agents in animal sector will be realized in 50% in provinces (autonomous regions and municipalities).
✓ To optimize the surveillance networks of AMU and AMR. To set up reference laboratories of antimicrobial resistance and bacterial strain banks. To establish evaluation system for AMU and AMR.
✓ The antimicrobials shared by humans and animals or easily producing cross-resistance should be gradually withdrawn from the market of animal growth promoter. To effectively control the increasing trend of the main animal origin antimicrobial-resistant bacteria.
✓ To develop and implement educational efforts to ensure that medical staff, veterinarians and animal producers receive information and training of rational use of antibacterial agents.
National action plan to contain antimicrobial resistance of animal origin (2017—2020年)  
(draft for comments)
Part 1 Preface

Part 2 Goals

Part 3 Key Tasks
- Gradual withdrawal project of veterinary antimicrobials as growth promotion
- Clinical application supervision project of veterinary antimicrobials
- Veterinary antimicrobial resistance monitoring project
- Residue control project of veterinary antimicrobials
- Demonstration project of reducing the use of veterinary antimicrobials
- Practitioner training and public education project

Part 4 Capacity Building
- Informatization Capability
- Standardization Capability
- Science and technology support
- International cooperation ability

Part 5 Guarantee Measures
Supplementation of antimicrobials, especially the antibiotic raw materials, to feed by fish feed enterprises will be punished severely. Other illegal actions, such as the use of human antibiotics, hormone and drugs on the list of forbidden aquaculture drugs will also be punished.
Specific the aquaculture sector, the following works were done

✔️ Have issued a “pilot action plan for reducing antimicrobial consumption in aquaculture”
  • Establish and implement operating procedures for disease prevention and control
  • Carry out surveillance of AMR of fish pathogenic bacteria
  • Advocate and guide precise medication technology: timely and accurate disease diagnosis; right selection of antibiotic based on sensitivity testing of the pathogens; using appropriate dose at the right time; avoiding overdose and extended treatment course; prohibiting prophylactic antibiotics use and being used as growth promoter.
Daily isolation and identification of pathogenic bacteria, and antibiotic sensitivity test are performed in “aquatic animal disease prevention stations” in some counties and provincial fisheries technology extension stations and other laboratories to help choosing the antibiotic that will be most effective against the specific types of bacteria in the shortest time.

Edit and publish technical manuals
Application of Probiotics in Aquaculture

National Registered Fishery Drugs and Medication Technology

Medication Guideline for the Prevention of Fish Diseases

• Investigation Report on Fishery Drugs Industry and its Management
✓ Encourage, explore and experiment antibiotics-free fish farming related technologies.
✓ promote the use of alternatives to antibiotics, such as herbal medicine, probiotics, vaccine, immunostimulants, egg yolk antibody, organic acid, and so on.
Innovating and popularizing new cultivation technologies. This is the key to reduce AMU and AMR in aquaculture

- Integrated multi-trophic aquaculture (IMTA)
- Integrated ecological fishery such as Rice Field Integrated Farming of different aquatic animals, such as fish plus crayfish, and so on.
- Application of microporous aeration technology
- Industrialized recirculating aquaculture system (RAS)
- Deep-sea cage farming technology
- Bioflocs technology in shrimp culture
- Multiple-trait selection technology of aquatic animals
- Development of high-throughput quick diagnosis technology
- Progress on vaccine technology
Conducting a governmental project on the AMR surveillance and monitoring in aquaculture from 2015

- National Fisheries Technology Extension Centre, Ministry of Agriculture, is the department in charge of this work
- This surveillance covered some aquaculture spots in 11 provinces which are the major aquaculture producers.
- The isolation and identification of the bacteria, and antibiotic sensitivity testing were done by the corresponding fisheries extension centers/stations in the provinces.
• There are still many aspects for improvement in this work. For example, we should more carefully choose the representative sampling locations and time, aquatic animal species, bacterial species so that we can obtain the truest reflection of AMR status in our country. For this purpose, we need to standardize the monitoring and testing protocols and strengthen the capacity building and technical training of all participating labs.
• In addition to the governmental AMR monitoring project mentioned above, there are many independent researches who conducted the survey of AMR of pathogenic bacteria isolated from aquatic animals. Because their results obtained by different investigators differ greatly, we can’t draw a conclusive evaluation on the status of AMR in China.
MIC of nine antimicrobials against 129 strains of miscellaneous bacteria isolated from cultured aquatic animals from coastal regions in Jiangsu province

From Qiao et al, 2015
Detection rate of various kinds of R gene from 90 strains of *Aeromonas* spp. collected from coastal areas in Jiangsu province

<table>
<thead>
<tr>
<th>R gene</th>
<th><em>A. veronii</em></th>
<th><em>A. hydrophila</em></th>
<th><em>A. sobria</em></th>
<th>other <em>Aeromonas</em></th>
<th>overall (Aeromonas spp.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TEM</td>
<td>0(0/41) *</td>
<td>0(0/25)</td>
<td>0(0/13)</td>
<td>0(0/11)</td>
<td>0(0/90)</td>
</tr>
<tr>
<td>IMP</td>
<td>2.44(1/41)</td>
<td>16(4/25)</td>
<td>7.69(1/13)</td>
<td>0(0/11)</td>
<td>6.67(6/90)</td>
</tr>
<tr>
<td>AmpC</td>
<td>34.15(14/41)</td>
<td>36(9/25)</td>
<td>61.54(8/13)</td>
<td>54.55(6/11)</td>
<td>41.11(37/90)</td>
</tr>
<tr>
<td>OXA-23</td>
<td>9.76(4/41)</td>
<td>0(0/25)</td>
<td>0(0/13)</td>
<td>0(0/11)</td>
<td>4.44(4/90)</td>
</tr>
<tr>
<td>aac(6’)-Ib</td>
<td>63.41(26/41)</td>
<td>72(18/25)</td>
<td>76.92(10/13)</td>
<td>63.64(7/11)</td>
<td>67.78(61/90)</td>
</tr>
<tr>
<td>ant(3’)-Ia</td>
<td>29.27(12/41)</td>
<td>28(7/25)</td>
<td>53.85(7/13)</td>
<td>27.27(3/11)</td>
<td>32.22(29/90)</td>
</tr>
<tr>
<td>aac(3)-IIa</td>
<td>4.88(2/41)</td>
<td>16(4/25)</td>
<td>15.38(2/13)</td>
<td>0(0/11)</td>
<td>8.89(8/90)</td>
</tr>
<tr>
<td>Sul1</td>
<td>36.59(15/41)</td>
<td>28(7/25)</td>
<td>30.77(4/13)</td>
<td>45.45(5/11)</td>
<td>34.44(31/90)</td>
</tr>
<tr>
<td>Sul3</td>
<td>51.22(21/41)</td>
<td>32(8/25)</td>
<td>53.85(7/13)</td>
<td>45.45(5/11)</td>
<td>45.56(41/90)</td>
</tr>
<tr>
<td>tetA</td>
<td>31.71(13/41)</td>
<td>20(5/25)</td>
<td>53.85(7/13)</td>
<td>36.36(4/11)</td>
<td>32.22(29/90)</td>
</tr>
<tr>
<td>tetC</td>
<td>34.15(14/41)</td>
<td>24(6/25)</td>
<td>53.85(7/13)</td>
<td>36.36(4/11)</td>
<td>34.44(31/90)</td>
</tr>
<tr>
<td>tetM</td>
<td>60.98(25/41)</td>
<td>48(12/25)</td>
<td>84.62(11/13)</td>
<td>54.55(6/11)</td>
<td>60(56/90)</td>
</tr>
<tr>
<td>floR</td>
<td>90.24(37/41)</td>
<td>48(12/25)</td>
<td>84.62(11/13)</td>
<td>81.82(8/11)</td>
<td>76.67(69/90)</td>
</tr>
<tr>
<td>qnrA</td>
<td>2.44(1/41)</td>
<td>4(1/25)</td>
<td>7.69(1/13)</td>
<td>0(0/11)</td>
<td>3.33(5/90)</td>
</tr>
<tr>
<td>qnrB</td>
<td>46.34(19/41)</td>
<td>60(15/25)</td>
<td>53.85(7/13)</td>
<td>54.55(6/11)</td>
<td>52.22(47/90)</td>
</tr>
<tr>
<td>qnrB-24</td>
<td>58.54(24/41)</td>
<td>32(8/25)</td>
<td>53.85(7/13)</td>
<td>27.27(3/11)</td>
<td>46.67(42/90)</td>
</tr>
<tr>
<td>qnrS</td>
<td>43.90(18/41)</td>
<td>12(3/25)</td>
<td>15.38(2/13)</td>
<td>9.09(1/11)</td>
<td>26.67(24/90)</td>
</tr>
<tr>
<td>qepA</td>
<td>70.73(29/41)</td>
<td>32(8/25)</td>
<td>61.53(8/13)</td>
<td>27.27(3/11)</td>
<td>53.33(48/90)</td>
</tr>
</tbody>
</table>

* Detection rate/ No. of strains; from Qiao et al, 2015
The following Stakeholders should be involved in this aquatic AMR project:

- Government: policy maker and budget provider
- Fisheries technology extension setups: organizer
- Academe: technology provider
- Fish medicine producers: antibiotic production & distribution information provider
- Fish farmers: antibiotics users, and supporter for sampling and information (type, dosage, efficacy, etc) collection.
Challenges related to AMR survey

- How to decide the sampling sites (for bacteria isolation). The sampling locations should be fixed every year?
- Only pathogenic bacteria will used to determine MIC? But if there is no disease outbreak, it is difficult to obtain the target species
- Criteria for determining susceptible, intermediate, and resistant breakpoints for dilution and disk diffusion methods.
- Need to standardize and harmonize MIC testing method for aquatic isolates.
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Ms. Wang Jing
Prof. Wang Yutang
Dr. Zhang Qianqian
Thank you very much for your attention

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