ANTIBIOTICS IN FISH AND FISHERY PRODUCTS

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Introduction

> "The increasing problems associated with infectious diseases in fish, the limited number of drugs available for treatment and prevention of these diseases, and the rapid increase in resistance to these antibiotics represent major challenges for this source of food production worldwide." - American Society of Microbiology Task Force on Antibiotic Resistance (ASM 1994)

Antibiotics are naturally-occurring, semi-synthetic and synthetic compounds with antimicrobial activity that can be administered orally, parenterally or topically are used in human and veterinary medicine to treat and prevent disease, and for other purposes including growth promotion in food animals. Antibiotic resistance is as ancient as antibiotics, protecting antibiotic-producing organisms from their own products, and other originally susceptible organisms from their competitive attack in nature. All antibiotics can select spontaneous resistant mutants and bacteria that have acquired resistance by transfer from other bacteria. These resistant variants, as well as species that are inherently resistant, can become dominant and spread in host-animal populations. The more an antibiotic is used, the more likely are resistant populations to develop among pathogens and among commensal bacteria of an increasing number of animals in an exposed population. However, there is great diversity: whereas some bacteria very rapidly develop resistance in the individual treated, others remain susceptible.

Significance of antibiotics

Antibiotics are drugs of natural or synthetic origin that have the capacity to kill or to inhibit the growth of micro-organisms. Antibiotics that are sufficiently non-toxic to the host are used as chemotherapeutic agents in the treatment of infectious diseases of humans, animals and plants. They have long been present in the environment and have played a crucial role in the battle between man and microbe. Many bacterial species multiply rapidly enough to double their numbers every 20-30 minutes, so their ability to adapt to changes in the environment and survive unfavorable conditions often results in the development of mutations that enable the species to survive changing external conditions.

The indiscriminate use of antibiotics for veterinary purposes has increasingly become a matter of public concern, and legal requirements are being reinforced. Regulatory authorities license antibiotics for use if the agents meet scientific criteria for quality, efficacy and safety. The authorities have to consider safety in relation to the treated animal, to the consumer and to the individuals handling the product during treatment.

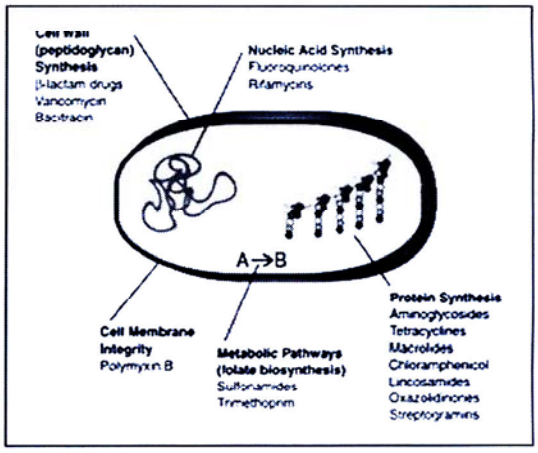
In the fish farming (aquaculture, mariculture, etc.) sector, the widespread use of antibiotics for treating bacterial diseases has been associated with development of antibiotic resistance in *Aeromonas hydrophila*, *A. salmonicida, Edwardsiella tarda, E. icttaluri*, *Vibrio anguillarum, V. salmonicida, Pasteurella piscida* and *Yersinia ruckeri* and controlled studies are needed to determine the effect of antimicrobial therapy on the ecology of aquaculture ponds, particularly at the micro-organism level. The contribution to antimicrobial resistance of antibiotics used in the aquaculture industry is reviewed in this work, using a risk analysis framework. Some recommendations on responsible conduct in this context are proposed, aimed at diminishing the antimicrobial resistance threat

As per *Regulation EEC 2377/90,* Residues of veterinary medicinal products means all pharmacologically active substances, whether active principles, excipients or degradation products, and their metabolites which remain in foodstuffs obtained from animals to which the veterinary medicinal product in question has been administered.

MECHANISM OF ACTION OF ANTIBIOTICS

Inhibition of cell wall synthesis:

Bacteria cell wall unique in construction, which contain a predominant compound called peptidoglycan. Antimicrobials that interfere with the synthesis of cell wall do not interfere with eukaryotic cell due to the lack of cell wall in animal cells and differences in cell wall in plant cells. These drugs have very high therapeutic index and low toxicity with high effectiveness. Antimicrobials of this class include, β lactam drugs, Vancomycin , Bacitracin etc



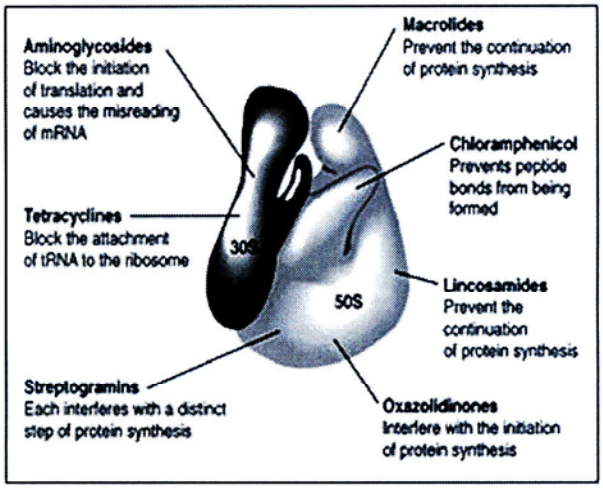
Penicillins and cephalosporins are part of group of drugs called β –lactams. They are called so because they have a shared chemical structure called β-lactam ring. These antibiotics competitively inhibit the function of penicillin-binding proteins and inhibit peptide bridge formation between glycan molecules. This causes the cell wall to develop weak points at the growth sites and become fragile. The weakness in the cell wall causes the cell to lyse.

Inhibition of protein synthesis

Structure of prokaryotic ribosome acts as target for many antimicrobials of this class. Differences in prokaryotic and eukaryotic ribosomes are responsible for selective toxicity. Drugs of this class include Aminoglycosides, Tetracyclins , Macrolides, Chloramphenicol etc

Aminoglycosides, irreversibly binds to 30S ribosomal subunit of the cell and causes distortion and malfunction of ribosome, which results in blockage of initiation translation. This causes misreading of mRNA and examples of aminoglycosides include Gentamicin, streptomycin and tobramycin. Side effects with extended use include, Otto toxicity, Nephrotoxicity etc

Tetracyclines on the other hand, reversibly bind 30S ribosomal subunit of the cell, which blocks attachment of tRNA to ribosome and prevents continuation of protein synthesis. This antibiotics is effective against certain Gram +ve and Gram –ve bacteria. This antibiotic may cause discoloration of teeth if administered to young children.



Macrolides include Erythromycin, clarithromycin and azithromycin. They reversibly binds to 50S ribosome and Prevents continuation of protein synthesis. These are effective against variety of Gram +ve organisms and those responsible for atypical pneumonia, often drug of choice for patients who are allergic to penicillin.

Chloramphenicol acts in a similar way, it binds to 50S ribosomal subunit and prevents peptide bonds from forming and blocking proteins synthesis. This is very effective against a wide variety of organisms. This drug is generally used as drug of last resort for life-threatening infections. Rare but lethal side effect is aplastic anaemia

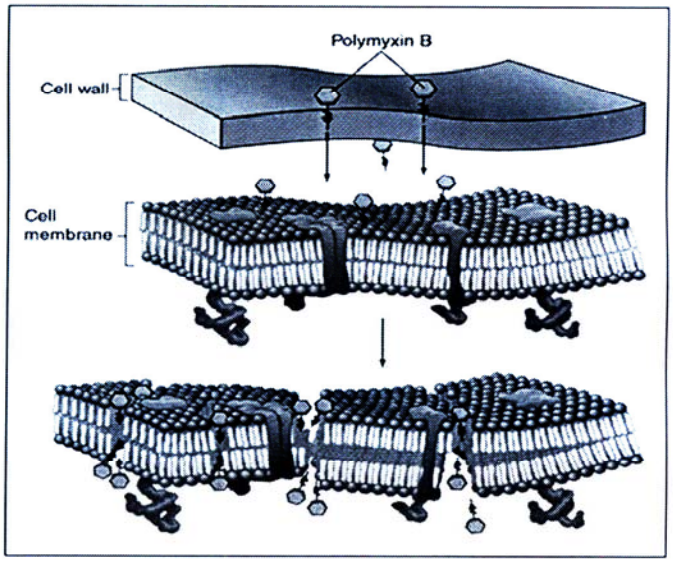
Inhibition of nucleic acid synthesis

The antibiotic in this class include Fluoroquinolones and Rifamycins. Fluoroquinolones inhibit action of topoisomerase DNA gyrase in the cell, which is responsible for maintaining supercoiling of DNA. The antibiotics in this group include Ciprofloxacin and ofloxacin

Rifamycins acts by blocking prokaryotic RNA polymerase and thereby preventing initiation of transcription. Rifampin is most widely used rifamycins and is effective against many Gram +ve and some Gram -ve as well as members of genus Mycobacterium. Primarily used to treat tuberculosis and Hansen's disease as well as preventing meningitis after exposure to *N. meningitidis*

Interference with cell membrane integrity

This class of antibiotics acts by creating damages cell membrane. The most common antibiotic in this class is Polymixn B, which is a common ingredient in first-aid skin ointments. This will bind with membrane of Gram-cells, and subsequently alters permeability of the membrane and thus leads to leakage of cell and cell death. Sometimes this antibiotic also binds eukaryotic cells but to lesser extent. The use of this class of antibiotic is limited to topical applications.



The use of antibiotics in food animals

The National Committee for Clinical Laboratory Standards (NCCLS) has defined terms to describe herd or flock antibiotic use. Therapy is the administration of an antimicrobial to an animal, or group of animals, which exhibit frank clinical disease. Control is the administration of an antimicrobial to animals, usually as a herd or flock, in which morbidity and/or mortality has exceeded baseline norms. Prevention/prophylaxis is the administration of an antimicrobial to exposed healthy animals considered to be at risk, but before expected onset of disease and for which no etiological agent has yet been cultured. (Metaphylaxis is a term sometimes used when there is clinical disease in some animals, but all are treated.) Growth promotion is the administration of an antimicrobial, usually as a feed additive, over a period of time, to growing animals that results in improved physiological performance.

The typical mode of action of antibiotics can be summarized as follows:

Typical modes of action of common antibiotics.

Mechanism	Comments	Examples
Damage cell membrane, allowing contents to leak out. Bactericidal.	High toxicity to animals and humans; topical use only	polymixins.
Inhibitors of bacterial cell wall synthesis.	Animals and humans not affected because their cells do not have walls.	penicillins; aminopenicillins; cephalosporins (cephalexin); bacitracin (topical); vancomycin.
Inhibitors of folic acid synthesis. Folic acid is needed to make RNA and DNA for growth and multiplication, and bacteria must synthesize folic acid. Bacteriostatic.	Animals and humans obtain folic acid from their diets, so they are not affected.	sulphonamides; sulfasalazine; trimethoprim; co-trimoxazole.
Inhibitors of DNA function. DNA is needed for cell growth and division. Most are bactericidal.	Drugs used affect bacterial (or fungal) cells more than animal or human cells.	nalidixic acid; ofloxacin; metronidazole; rifampin; enrofloxacin; sarafloxacin
Inhibitors of protein synthesis. Proteins are synthesized on cell Structures called ribosomes. Bactericidal or bacteriostatic.	High doses can affect animals and humans because some ribosomes are similar to those in bacteria.	tetracyclines; aminoglycosides; chloramphenicol; florfenicol; macrolides; spectinomycin; lincosamides.

Therapy, control and prevention:

When antibiotic treatment is necessary, it often has to be administered to food animals in feed or water. Individual animal treatment is almost never practical for poultry, but may be practical for cattle and swine.

In livestock production, the objective is to limit progression of disease in the population, since illness decreases animal performance. Herd or flock treatment is often indicated

when illness is first recognized in a small proportion of the animals. For example, one of the indications for the use of antibiotics in animals is physical stress involved, for example, in the movement of animals in large numbers. Whereas mass regimens can improve animal performance and the general welfare of the treated animals, such regimens do result in increased antimicrobial usage. Mass treatment programmes generally err on the side of administering treatment to individuals that do not need it (as occurs in prophylaxis in human medicine), whereas limitation of therapy to recognized clinical cases errs on the side of withholding treatment from some individuals that would benefit. Attempts to limit mass metaphylaxis to those individual animals most likely to benefit, using rectal temperature as a clinical indicator for treatment, have usually been unsuccessful. More sophisticated measures of disease status are being investigated as one means to improve treatment selection criteria.

Growth promotion:

The growth promoting effects of antibiotics were first discovered in the 1940s when chickens fed by-products of tetracycline fermentation were found to grow faster than those that were not fed those by-products. Since then, many antimicrobials have been found to improve average daily weight gain and feed efficiency in livestock in a variety of applications, and this is known as 'growth promotion'.

The feeding of antibiotics is associated with decreases in animal gut mass, increased intestinal absorption of nutrients and energy sparing. This results in a reduction in the nutrient cost for maintenance, so that a larger portion of consumed nutrients can be used for growth and production, thereby improving the efficiency of nutrient use. Antibiotics act by eliminating the subclinical population of pathogenic micro- organisms. Eradicating this metabolic drain allows more efficient use of nutrients for food production. Antibiotics alter the non-pathogenic intestinal flora, producing beneficial effects on digestive processes and more efficient utilization of nutrients in feeds. It has been estimated that around 6 percent of the energy in a pig's diet could be lost due to microbial fermentation occurring in the stomach and small intestine

Antibiotics banned for animals intended for food production

Antibiotics which are banned for use in animals which are intended as our food are many. This has happened mainly because; the residue of the antibiotic will remain in the meat and will result in the development of antimicrobial resistance in humans and other reactions. For example, Chloramphenicol is a potent, broad-spectrum antibiotic used only at therapeutic doses for treatment of serious infections in humans. Due to the unpredictable effects of doses on different patient populations, it has not been possible to identify a safe level of human exposure to Chloramphenicol. Therefore, United States of America Federal regulations prohibit its use in food-producing animals and animal-feed products. According to the European Medicines Agency (EMEA) a number of antibiotics are no longer available for use in veterinarian medicine. The other antibiotics which are banned are listed in the Table.

Antibiotics banned for animals intended for food production.

Antibiotic	*Country*	*Reason*	*Reference*
Spectinomycin	USA	Its use is limited by the ready development of bacterial resistance	USP, 2000d.
Enrofloxacin	USA	Its use is limited by the ready development of bacterial resistance (quinolone)	USP, 2000h.
Chloramphenicol	Argentina, Canada, EU, Japan, USA, India	Induces human aplastic anaemia	USP, 2000e; GESAMP, 1997; SANCO, 2001a.
Nitrofurans	Argentina, Canada, EU, Japan, USA, India	Carcinogenicity and mutagenicty	USP, 2000e; GESAMP, 1997; SANCO, 2001a
Rifampin	Not labeled in USA or Canada for use in animals, including food-producing animals	Tumorgenicity and teratogenic effects on experimental animals	USP, 2000k.

However, the following antibiotics were permitted for use in aquaculture by FAO.

ANTIBIOTICS AUTHORIZED FOR USE IN AQUACULTURE

Antibiotic	Treatment of	Reference
Oxytetracycline (for medicated feed)	• Furunculosis in salmonids (salmon or trout) caused by Aeromonas • Gafkemia in lobsters (caused by *Aerococcus viridans*). • Hemorrhagic septicaemia due to *Aeromonas hydrophila*, *A. sobria* and Pseudomonas. • Cold water disease in salmonids, caused by *Cytophaga psychrophilia.* • Columnaris disease in salmonids, caused by susceptible *Chondrococcus* (*Flexibacter*) columnaris. • Enteric redmouth disease, caused by susceptible *Yersinia ruckeri.* • Indicated for the control of Pseudomonas disease in catfish and salmonids. • Indicated for the control of ulcer disease caused by susceptible *Haemophilus piscium* in salmonids (salmon, trout).	USP, 2000g

Florfenicol Premix	Indicated in the treatment of furunculosis caused by susceptible strains of *Aeromonas salmonicida.*	USP, 2000f
Sarafloxacin	Indicated in the treatment of furunculosis, vibriosis and enteric redmouth in *Salmonidae.*	EMEA, 1997
Erythromycin	In the treatment of bacterial kidney disease (*Renibacterium salmoninarum*) and Streptococcosis in yellowtail in Japan.	GESAMP, 1997
Sulphonamides potentiated with trimethoprim or ormethoprim	Against furunculosis, enteric redmouth disease and vibriosis.	GESAMP, 1997

List of antibiotics and pharmacologically active substances, which are banned in India for use in aquaculture, is given below

S.No.	Antibiotics and other Pharmacologically Active Substances	Maximum Permissible Residual Level in ppm
1.	Chloramphenicol	Nil
2.	Nitrofurans including: Furaltadone, Furazolidone, Furylfuramide, Nifuratel, Nifuroxime, Nifurprazine, Nitrofurantoin, Nitrofurazone	Nil
3.	Neomycin	Nil
4.	Nalidixic acid	Nil
5.	Sulphamethoxazole	Nil
6.	Aristolochia spp and preparations thereof	Nil
7.	Chloroform	Nil
8.	Chlorpromazine	Nil
9.	Colchicine	Nil
10.	Dapsone	Nil
11.	Dimetridazole	Nil
12.	Metronidazole	Nil
13.	Ronidazole	Nil
14.	Ipronidazole	Nil
15.	Other nitroimidazoles	Nil
16.	Clenbuterol	Nil
17.	Diethylstilbestrol (DES)	Nil
18.	Sulfonamide drugs (except approved Sulfadimethoxine, Sulfabromomethazine and Sulfaethoxypyridazine)	Nil
19.	Fluroquinolones	Nil
20.	Glycopeptides	Nil

Proceedings of the Meeting of the Expert Group Organised by Aquaculture Authority, Government of India on the Use of Antibiotics, Drugs and Chemicals in Shrimp Aquaculture and Steps to be taken for their Regulation

Incidence of antibiotics, antibiotic residues in fish and fishery products and fishery environments

Although most countries have banned the antibiotics chloramphenicol and nitrofurans from animal food production due to their toxicity to humans, traces of the drugs have been detected in shrimp and other aquaculture products. Chloramphenicol can cause potentially

fatal aplastic anemia and leukemia, and nitrofurans are carcinogenic. Therefore, the seafood industry fully supports regulations that control the drugs to assure wholesome foods for consumers.

At issue in the current antibiotic residue debate is the distinction between detection and toxicity. Advancing analytical technology is allowing detection of substances at ever-diminishing levels. For example, heavy metals, pesticides and carcinogens can be highly toxic, yet are found in virtually all wholesome foods at trace levels. Studies have shown that such low levels are innocuous. With increasing analytical capability, it is unrealistic to expect foods to be free of any detectable level of hazardous substances.

In order to determine the point at which a hazardous substance presents a health risk, food safety experts have developed the concept of the maximum residue limit (MRL).and Minimum Required Performance Limit (MRPL) – for banned substances. This is the amount of residue considered to have no significant toxicological risk for human health. MRLs are based on "acceptable daily intakes," which in turn are typically based on "no observable adverse effects" levels derived from animal and *in vitro* trials.

Environmental Contamination

Increasing human population is contributing greater contamination to global water bodies. A recent study by the United States Geological Survey analyzed water samples from 139 streams across 30 states. Results indicated the presence of antibiotics in 48% of the samples at combined residual levels of 3.6 ppb.

The existence of such pervasive environmental contamination implies that it will not be possible to completely eliminate antibiotic residues from aquaculture products, even if antibiotic usage by aquaculture is completely stopped. Indeed, preliminary analyses of a variety of sea-caught products, as well as terrestrial animal foods revealed traces of chloramphenicol and nitrofurans.

The risks from antibiotic residues are well-known and detectable but the case makes several points in relation to emerging risk. One, it is possible that science causes hazards to 'emerge' (rise in significance) as a result of improved detection methods. Two, an identified hazard in an industry could flag for other potential concern.

In the case of aquacultured shrimp, the rapid rise of EU imports from Southeast Asia and China may have indicated emerging food safety problems. The reasoning behind a signal of rapid increases in export flow and production is that the innovations required to expand supply might introduce risk into the process. In the case of shrimp aquaculture in Southeast Asia, most of the supply expansion in shrimp aquaculture from the 1980s on has been the result of productivity growth. Although some additional water and land (and labour) resources have been brought into shrimp farming, the biggest effect has come from an intensification of aquaculture activity. As a result, the disease pressure in shrimp production increased, some pathogens spreading easily amongst the shrimp population.

Heavy application of antibiotics was the main preventive measure, resulting in food safety problems of two kinds: antibiotic resistant bacterial strains in the environment resistance, and residues of veterinary medicine on the shrimp resulting in a possible toxic effect from human consumption.

Shrimp imports from Southeast Asia, including India and China, into the EU more than tripled over the one and a half decade between 1998 and 2003. Total imports from the Top 4 Southeast Asian exporters (Indonesia, Malaysia, Vietnam and Thailand) India and China into the EU amounted to nearly 70 million tons in 2004.Thailand was the main supplier of shrimp in the EU in the late 1980s and early 1990s but never fully recovered from an outbreak of shrimp disease in 1995. This proved a major stimulus for competing traders from China, Malaysia and Indonesia. After the breakdown year 2002, which followed the detected contamination of chloramphenicol and nitrofurans in Asian shrimp in 2001, exports from Indonesia and Malaysia swiftly recovered while other countries stagnated.

In 2002, the EU implemented the so-called "zero tolerance" policy regarding antibiotics residue. Using the high performance liquid chromatography (HPLC) method, the EU laboratories are equipped to detect traces of prohibited carcinogenic antibiotics like chloramphenicol up to 0.3 ppb and nitrofuran up to 1 ppb levels. Some of the EU regulations, for instance, for detecting mercury, are close to being non-detectable.

According to the Seafood Exporters Association of India (SEAI), since February 2002, there have been several cases of rejection of Indian shrimp imports into the EU market on account of detecting traces of nitrofuran and Chloramphenicol as well as other bacterial inhibitors like amino-glycosides and macrolides. As a result of such stringent standards (which are clearly very difficult to meet by a developing country like India), in 2004, India still remained in List 1 of Annex 1 of the EC Decision 97/276/EC, amended by 99/136/EC, whereby all organizations exporting seafood to the EU require export-worthy certification of their processing facilities by an EU-nominated inspection agency. Around the same time, Japan – the last of the three major seafood importing nations from India – also imposed strict standards on shrimps imported from India in 2002, and made it mandatory for consignments to be accompanied by a certificate stating that the material was free of antibiotics, especially nitrofurans. Japan also refused consignments of shrimp produced in aquaculture on the east coast of India on account of their muddy smell.

Constructing signals from risk data

EU: data on notifications of chemical hazards can be easily noted on RASFF. The rapid alert system for food and feed (RASFF) data are a database operated by the European Food Safety Authority (EFSA), which support an early warning system with the cooperation of the countries in Western Europe. The purpose of RASFF is to share information on topical and prospected food hazards among the contributing countries, which are the EU and other countries in northwest Europe. What information on emerging risk is contained in RASFF data?

Hazard awareness among the member countries

RASFF, or any other source of product detention or risk data, reflects the cumulative and scientific knowledge on hazards that are acknowledged. It measures those hazards in the food chain on which there is *general* awareness in the body of European scientists that advise EFSA.

Prevention of Hazardous trade

Data entered in the RASFF database as product-market-hazard combinations that warn risk authorities essentially on the potential entry of hazardous trade flows into their territories, not on the emergence of hazards per se. The hazards never encountered at inspection -because proper preventive measures are in place and do not appear in the database.

Table 3. Summary of SEM notification data

Crustaceans and products thereof	
Number of notifications	227
Range of contamination (min–max, µg/kg – ppb)	0.44–7 500
Contamination > 5 µg/kg – ppb (No.)	125
> 10 µg/kg – ppb (No.)	51
> 1 000 µg/kg – ppb (No.)	7
Countries of origin	No. of products
Bangladesh	112
Brazil	1
China	6
India	68
Madagascar	1
Malaysia	1
Myanmar	1
Sri Lanka	6
Thailand	26
Vietnam	5
Eggs and egg products	
Number of notified analyses	4
Range of contamination (min–max, µg/kg – ppb)	1.0–2.4
Countries of origin	No. of products
Brazil	1
France	1
India	1
Israel	1
Farmed crustaceans and products thereof – (obsolete)	
Number of notified analyses	27
Range of contamination (min–max, µg/kg – ppb)	0.6–24.0
Contamination > 5 µg/kg – ppb (No.)	14
> 10 µg/kg – ppb (No.)	4
Countries of origin	No. of products
Bangladesh	15
India	9
Thailand	2
Vietnam	1
Fish and products thereof	
Number of notified analyses	8
Range of contamination (min–max, µg/kg – ppb)	1.0–122.0
Contamination > 5 µg/kg – ppb (No.)	3
> 10 µg/kg – ppb (No.)	1
Countries of origin	No. of products
Bangladesh	1
China	2
Peru	3
Thailand	1
Vietnam	1
Food additives	
Number of notified analyses	2
Range of contamination (min–max, µg/kg – ppb)	> 1.00
Countries of origin	No. of products
Canada, Chile, Indonesia, Tanzania (sea weeds)	1
Italy	1
Honey and royal jelly	
Number of notified analyses	6
Range of contamination (min–max, µg/kg – ppb)	1.1–11.0
Contamination > 10 µg/kg – ppb (No.)	1
Countries of origin	No. of products
Hungary	3
China	1
India	2
Meat and meat products (other than poultry)	
Number of notified analyses	16
Range of contamination (min–max, µg/kg – ppb)	0.1–14.4
Contamination > 5 µg/kg – ppb (No.	5
> 10 µg/kg – ppb (No.)	1
Countries of origin	No. of products
Brazil	1
China	13
Indonesia	2
Poultry meat and poultry meat products	
Number of notified analyses	37
Range of contamination (min–max, µg/kg – ppb)	0.5–47.0
Contamination > 5 µg/kg – ppb (No.)	21
> 10 µg/kg – ppb (No.)	20
Countries of origin	No. of products
Brazil	16
The Netherlands	1
Thailand	20
Wild caught crustaceans and products thereof – (obsolete)	
Number of notified analyses	17
Range of contamination (min–max, µg/kg – ppb)	0.4–19.3
Contamination > 5 µg/kg – ppb (No.)	4
> 10 µg/kg – ppb (No.)	3
Countries of origin	No. of products
Bangladesh	1
India	2
China	7
Thailand	7
Wild caught fish and products thereof (other than crustaceans and molluscs) – (obsolete)	
Number of notified analyses	1
Range of contamination (min–max, µg/kg – ppb)	0.3
Countries of origin	No. of products
Thailand	1

HACCP vis-à-vis prevention / control strategies for the prevention of antibiotics in fish and fishery products.

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

As the fact goes, the processors should clearly understand that antibiotics once got into their product, cannot be removed by any known methods. So only option they have is to receive raw material which do not have any residue of antibiotics. So what are the control measures?

To control this hazard in food animals, all drugs, whether for direct medication or for addition to feed, must be approved by competent authority. Incentives for the use of animal drugs in aquatic animal species include the need to: 1) treat and prevent disease; 2) control parasites; 3) affect reproduction and growth; and, 4) tranquilization (e.g. during transit). Relatively few drugs have been approved for aquaculture. As a result, aquaculture growers may use unapproved drugs, general purpose chemicals that are not labeled for drug use, and approved drugs in a manner that deviates from the labeled instructions.

When a drug is approved by competent authority, the conditions of the approval are listed on its label. These conditions include: the species for which the drug is approved; the approved dosage; the approved route of administration; the approved frequency of use; and the approved indications for use including the withdrawal period. Only a licensed veterinarian / technologists may legally prescribe or use a drug under conditions that are not listed on the label.

Labels of approved drugs list mandatory withdrawal times, where applicable. These withdrawal times must be observed to ensure that the edible tissue is safe when it is offered for sale. Tissue residue tolerances have been established for some drugs (FDA, 2001).

Control Measures

Control measures for the control of aquaculture drugs used in aquaculture operations can include:

1. On-farm visits to review drug usage before receipt of the product, coupled with a supplier's lot-by-lot certificate that any antibiotic administered were used in conformance with the application requirements.
2. Receipt of supplier's lot-by-lot certification of proper drug usage, coupled with appropriate verification.
3. Review of drug usage records kept at the farm by auditing the farm periodically and at receipt of the product, coupled with a supplier's lot-by-lot certificate that any drug used were used in conformance with the application requirements.
4. Drug residue testing.
5. Receipt of evidence (e.g. third party certificate) that the producer operates under a third party- audited Quality Assurance Program for aquaculture drug use.
6. Observation of required withdrawal period.

Conclusion:

Most of the chemicals used in aquaculture such as pesticides and antibiotics to ponds can be bio-accumulative and present a food safety hazard. By adopting HACCP and Good Management practices, we can prevent potential problems from aquaculture. Aquaculture farmers who use these substances should follow product labels regarding dosage, withdrawal period, proper use, storage, disposal and other constraints including environmental and human safety precautions. Records should be maintained properly regarding the type of chemical used, its source, the quantity and withdrawal period observed. The adoption of HACCP and GMP by aquaculturists is a practical way to tackle this hazard and to show case our products to the international community as a safe and high quality product.