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Joint Group of Experts on the
Scientific Aspects of Marine Environmental Protection
- GESAMP -

TOWARDS SAFE AND EFFECTIVE USE OF CHEMICALS IN COASTAL AQUACULTURE

FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS

Rome, 1997

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PREPARATION OF THIS STUDY

This study has been prepared on the basis of the work of the GESAMP Working Group on Environmental Impacts of Coastal Aquaculture.

The Working Group met in Iloilo, Philippines, 22 - 28 May 1996. Its report was reviewed by the 27th session of GESAMP, Nairobi, 14 - 18 April 1997, and subsequently approved for publication in its present form.

The Working Group session was attended by the following experts: David J. Aldermann, Uwe Barg (Technical Secretary), Mali Boonyaratpalin, Erlinda Cruz-Lacierda, Valerie Inglis, Celia Lavilla-Pitogo and Ewen MacLean, Jurgene Primavera, Donald P. Weston (chair). A study was contributed by Palarp Sinhaseni, Malinee Limpoka and Omrat Samitawat. Donald Lightner, Michael Phillips, Marco Saroglia and Albert Tacon provided valuable comments on the draft prepared by the Working Group.

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EXECUTIVE SUMMARY

The chemicals used in coastal aquaculture include those associated with structural materials, soil and water treatments, antibacterial agents, other therapeutants, pesticides, feed additives, anaesthetics, and hormones. As the aquaculture industry has expanded, it has adopted chemicals originally developed for use in other sectors, most notably the agricultural sector. Consequently many chemicals now in common use in aquaculture have never been specifically evaluated from the perspective of their effects on the aquatic environment, particularly coastal waters. The purpose of this report is to provide an overview on chemical use in coastal aquaculture globally and the potential environmental and human health implications with the objective of promoting: (i) protection of coastal environments; (ii) protection of human health; and (iii) sustainability of the aquaculture sector.

Chemicals used within the aquaculture industry are identified and, for each chemical, a brief summary of information is provided, when available, on its intended purpose, scale of application, the aquacultural sectors and geographic locations of principal use and potential impacts on the environment and human health. Environmental issues arising from the properties of aquacultural chemicals are discussed. For example, environmental persistence is likely to be a prominent consideration in predicting fate and effects but is highly dependent on the specific chemical and local environmental conditions. Residues in non-cultured organisms have been documented for some antibacterials. Toxicity to non-target species can be a concern for certain pesticides. Stimulation of drug resistance in aquatic micro-organisms is a potential consequence of the use of antibacterials.

The possible effects of some aquacultural chemicals, particularly pesticides (e.g., organophosphates) and some therapeutants, on the health of fishfarm workers are of concern. Standard health and safety precautions will mitigate the risks involved and it is essential that employers and employees observe these precautions. Residues in seafood could pose a potential risk to consumers through hypersensitivity to drug residues or the emergence of antibacterial-resistant intestinal microflora.

The use of chemicals may incur penalties to the aquaculture industry including: (1) international trade difficulties arising from drug residue monitoring and enforcement programmes; (2) the potential for loss of efficacy of prophylactic antibacterial agents; and (3) increased demand for and complexity of effluent treatment. Such potential problems have to be considered in the context of the limited alternatives to chemotherapy that are available to the aquaculture industry. These problems and others are discussed and potential solutions identified.

Generally speaking, chemicals in use in aquaculture today can be grouped into three categories. The first consists of aquacultural chemicals that pose an inherently high level of hazard, and on this basis alone their use should be curtailed. This category includes chloramphenicol, organotin molluscicides, malachite green and, potentially, some organophosphates. The second category includes chemicals that can be used safely if standard precautions are followed but pose a threat to the environment and/or human health if misused. Excessive dosage, failure to provide for adequate neutralisation or dilution prior to discharge, or lack of adequate personal protection equipment are among the factors that could make the use of an inherently acceptable chemical unsafe. The third category of chemicals includes those that may be environmentally benign under most situations but detrimental at specific sites because of the unique attributes of such sites. Proper selection of farm sites can substantially reduce the environmental impacts of aquacultural chemicals.

Evaluation of the risks associated with aquacultural chemicals is complicated by the lack of quantitative data on their use. Most countries have no data on the amounts of chemicals used in aquaculture within their borders. Chemical manufacturers do not release this information and, in many cases, may not even know the ultimate use of their products. We also lack field data useful for quantifying risk such as the effluent concentrations of chemicals and the nature and extent of biological response in receiving waters. Relevant data are particularly limited for tropical areas. Most information on aquacultural chemicals (e.g., efficacy, metabolism, environmental fate) has been acquired under temperate conditions. Such information may, or may not, be applicable in lower latitudes where temperature, soil characteristics and the peculiar attributes of the principal cultured species make extrapolation from temperate data somewhat tenuous.

The viability of contemporary aquaculture is contingent on the use of chemicals. Accordingly, while the overriding consideration should be minimising the quantities of chemicals applied, most current uses of chemicals are essential. Recognising that chemotherapeutants and pesticides in current use are of varying effectiveness and hazard, recommendations are provided to promote the safe and effective use of chemicals in coastal aquaculture. Governmental authorities, the scientific community and the aquacultural and pharmaceutical industries all have important roles to play to ensure that chemical use is consistent with protection of environmental quality and human health. In particular, mechanisms need to be put in place and enforced for the registration and control of aquacultural chemicals to protect the environment and human health and to ensure the sustainable growth of the aquaculture industry.

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ABSTRACT

GESAMP (IMO/FAO/UNESCO-IOC/WMO/WHO/IAEA/UN/UNEP Joint Group of Experts on the Scientific Aspects of Marine Environmental Protection).
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The use of most chemicals in aquaculture, if carried out properly, can be regarded as wholly beneficial with no attendant adverse environmental effects or increased risks to the health of aquacultural workers. Concerns appear warranted, however, regarding the over-use and misuse of certain chemicals for which proper risk assessments with respect to the marine environment have not been conducted. A further legitimate concern and a barrier to conducting an exhaustive review of these practices is the lack of availability of quantitative data on contemporary chemical use in the aquaculture industry.

The viability of contemporary aquaculture is contingent on the use of chemicals. Accordingly, while the overriding consideration should be minimising the quantities of chemicals applied, most current uses of chemicals are essential. Recognising that chemotherapeutants and pesticides in current use are of varying effectiveness and hazard, recommendations are provided to promote the safe and effective use of chemicals in coastal aquaculture.

Governmental authorities, the scientific community and the aquacultural and pharmaceutical industries all have important roles to play to ensure that chemical use is consistent with protection of environmental quality and human health. In particular, mechanisms need to be put in place and enforced for the registration and control of aquacultural chemicals to protect the environment and human health and to ensure the sustainable growth of the aquaculture industry.

Key words: Aquaculture, Mariculture, Coast, Chemotherapeutants, Pesticides, Environmental Impact, Human Health

Towards Safe and Effective Use of Chemicals in Coastal Aquaculture

1. INTRODUCTION

1.1. Scope and purpose of this study report

Aquaculture is the farming of aquatic organisms, including fish, molluscs, crustaceans and aquatic plants (see FAO, 1990). Aquaculture production world-wide is growing rapidly, at an annual growth rate of about 9.4% during the period 1984 to 1994 (FAO, 1995a, 1996). Total world aquaculture production in 1994 was 25.5 million metric tonnes, valued at US$ 39,800 million representing 21.7% of total world fisheries production by weight. Asian aquaculture farmers contributed more than 90% of the world's total aquaculture production, and more than 75% of total aquaculture yield was produced in low-income food-deficit countries (LIFDCs).

The majority of finfish produced by aquaculture is produced in extensive and semi-intensive freshwater culture systems. In contrast, the bulk of farmed molluscs (4.38 million metric tonnes), crustaceans (1 million t) and aquatic plants (i.e., seaweeds, 6.87 million t) were produced in coastal areas. Coastal finfish culture in 1994 produced more than 966,000 tonnes.

A variety of chemicals are used in aquaculture for purposes such as sediment and water management, enhancement of natural aquatic productivity, transport of live organisms, feed formulation, manipulation and enhancement of reproduction, growth promotion, health management, processing and adding value to the final product. Major benefits are derived from using chemicals in aquaculture. Generally, production efficiency is increased and waste of resources is reduced and animal welfare enhanced. Chemicals are essential for increased and controlled production of seed in hatcheries, increased feeding efficiency, improvement of survival rates, control of pathogens and diseases and reduction in transport stress. Chemical needs are minimal in extensive and semi-intensive culture methods, often being limited to addition of fertiliser (e.g., manure), soil or water treatments (e.g., lime), and perhaps a pesticide (e.g., use of teaseed as a piscicide). These minimal chemical needs would be typical in finfish culture systems utilising low stocking densities of herbivorous or omnivorous fish, including carp, milkfish and tilapia species. Similarly, much shrimp culture is primarily based on extensive and semi-intensive farming practices. Bivalves and seaweeds are grown in extensive systems since these rely on the natural productivity of coastal waters.

There is, however, a general trend towards intensification of production methods, and the quest for production gains is often accompanied by a greater reliance on chemotherapeutants, feed additives, hormones, and more potent pesticides and parasiticides. Concern is growing over the use and potential misuse of some of these chemicals. The amount of information on chemical use in coastal aquaculture and its significance for human health assurance, environmental protection and sustainable development of the sector, has been increasing throughout the last decade (Rosenthal *et al.*, 1988; ADB/NACA, 1991; GESAMP, 1991; Michel and Alderman, 1992; Shariff *et al.*, 1992; Pullin *et al.*, 1993; Primavera *et al.*, 1993; ICES, 1994; FAO/NACA, 1995; Plumb, 1995; ADB/NACA, in press; SEAFDEC/FAO/CIDA, in press). Even so, information required for risk management is far from adequate. This report helps to fill one important gap by providing an overview of chemical use in coastal aquaculture practices world-wide. It also addresses the environmental and human health implications resulting from use of certain chemicals, with a view to promoting (i) protection of coastal environments, (ii) protection of human health, and (iii) sustainability of the aquaculture sector. The report is primarily intended for use by regulatory bodies. However, much of the information will also be useful to environmental scientists, aquaculturists, and chemical suppliers and producers.

1.2. Content of this study report

This report first provides a global overview of chemicals in use and their applications in coastal aquaculture (Section 2). The main issues of concern are addressed in Section 3. A discussion of major problems identified and their possible solutions is provided in Section 4. The final Section gives overall conclusions as well as general recommendations on the promotion of safe and effective use of chemotherapeutants and pesticides in coastal aquaculture.

2. CHEMICALS AND THEIR APPLICATIONS

Many countries engaged in coastal aquaculture have few regulatory controls and/or little documentation of the chemicals used by the industry. Even countries that maintain a list of approved chemicals and control their use rarely have information on the quantities actually applied. Consequently, the compilation of a complete and quantitative listing of aquaculture chemicals used world-wide is, at present, impossible. The need for mechanisms at national level to compile and maintain records on the types and quantities of chemicals used remains a high priority.

The following compilation of chemicals used in coastal aquaculture is based on literature available to, and personal knowledge of, the working group participants. Important sources of information included Michel and Alderman (1992), Alderman *et al.*, (1994) and SEAFDEC/FAO/CIDA (in press). A compounding problem with respect to cataloguing the variety of chemicals used globally relates to the lack of chemical use information for certain countries. However, it is assumed that in areas for which information is lacking, a great majority of chemicals used by the aquaculture industry would be the same as those used elsewhere in the world; they should therefore be included in the present list. Any chemicals omitted from the list are unlikely to be used either widely or in large quantities.

As the report focuses on coastal (i.e., marine and brackish water) aquaculture, any chemical used exclusively in freshwater aquaculture is not listed. For each chemical listed, we have, whenever possible and appropriate, provided information on:

- purpose of use;
- the main targets or beneficiaries of the application (*e.g.* species, system, life stage);
- a qualitative sense of the magnitude of use (*e.g.* widely used, infrequently used); and
- country or geographic region of use, if not widespread.

At the end of each chemical entry, publications specific to the properties (e.g., persistence, toxicity) and environmental behaviour and effects of the chemical, specific to aquacultural usage, are noted when available. The reader is also referred to Alderman *et al.* (1994) which provides a compilation of aquacultural chemicals, in many cases showing the chemical structure and including details on the purpose of use and therapeutic regimes (dose and duration).

Annex 1 provides hazard ranking profiles for those compounds described here and contained in the GESAMP 9.1 data base on harmful substances carried by ships, kept by the International Maritime Organization (IMO). These profiles, published periodically (see e.g., GESAMP, 1989), include information on bioaccumulation and toxicity to humans and aquatic animals. They were compiled for the purpose of developing standards and provisions for discharges at sea from ships' tank washings containing chemical residues, the safe carriage of packaged dangerous goods, and responses in case of accidental discharges. These profiles should not be used for other purposes without proper qualifications. Nevertheless, low ranking would indicate that aquacultural use of a substance is less likely to have significant environmental or human health effects, while high ranking would suggest that special care should be taken in using the chemical and that safer alternatives should be considered where available. It is important to recognise that, by their very nature, some aquacultural chemicals will have high rankings because therapeutants and pesticides would not be effective if they were not toxic to the pathogen or pest. These profiles do not, however, take into account the hazards posed to consumers by chemicals occurring as contaminants in aquaculture products.

2.1. Chemicals associated with structural materials

Structural materials, such as plastics, contain a wide range of additives including stabilisers (fatty acid salts), pigments, (chromates, cadmium sulphate), antioxidants (hindered phenols), UV absorbers (benzophenoles), flame retardants (organophosphates), fungicides and disinfectants. Although some protection is provided by their low water solubility, slow rate of leaching and dilution, many of these compounds can have adverse effects on aquatic life at low levels of exposure. Indeed, mortalities in aquaculture have resulted from chemicals leaching from plastic construction material (Zitko, 1986).

Antifoulants are used in coastal aquaculture throughout the world on solid surfaces and on net and rope structures. They increase the intervals between the manual or mechanical washing of such materials. Perhaps the best examples are the tributyltin (TBT) antifoulants first introduced in the mid 1960s. While initially developed for protection of boat hulls, TBT was also used to treat nets containing cultured fish. TBT residues have been found in cultured seafood products (Short and Thrower, 1986).

2.2. Soil and water treatments

Alum

Alum (potassium-aluminium sulphate) is widely used at concentrations of 10-20 mg/l as a flocculant to reduce turbidity in shrimp ponds.

EDTA

Disodium ethylenediaminetetraacetic acid (EDTA) chelates divalent and trivalent metal cations and is added to larval rearing water in some shrimp hatcheries in Southeast Asia and Latin America. The presence of EDTA will reduce the bioavailability of heavy metals by complexation.

Gypsum

Gypsum (calcium sulphate) is widely used at concentrations of 250-1000 mg/l as a flocculant to reduce turbidity in shrimp ponds.

Lime

Lime is widely used to neutralise acidity, increase total alkalinity, and to increase total hardness in the soil and water of grow-out ponds for fish and shrimp. The most common preparations/forms are agricultural limestone [calcite ($CaCO_3$) and dolomite ($MgCO_3$)], hydrated or slaked lime [$Ca(OH)_2$] and burnt lime or quick lime (CaO). During pond preparation, lime is applied to the pond bottom at doses of 100-8,000 kg/ha or to the water during the rearing period at 10-500 kg/ha. Liming is also practised (using different procedures) to neutralise acid sulphate resulting from oxidation of pyrites in ponds constructed in mangrove areas in Southeast and South Asia. Burnt lime is also used (at 50-100 g/m^2) in conjunction with ammonium phosphate to kill pests and predators.

Zeolite

Zeolites are tectosilicate minerals often applied at a dose of 100-500 kg/ha to shrimp ponds to remove ammonia. However, Boyd (1995) questions the efficacy of this procedure because (a) NH_4^+ adsorption is greatly repressed by high concentrations of dissolved cations in brackish water, and (b) cavities of zeolite fill with water and cannot absorb gases.

2.3. Fertilisers

Fertilisation is a standard practice during pond preparation to enhance production of natural food in ponds. The amount of fertiliser used decreases with the increase of intensity of culture. Extensive culture systems rely completely on the natural productivity of the ponds, thus they require inputs of fertiliser to enhance primary productivity. Intensive culture systems require less input of fertiliser, while relying heavily on the use of feeds. In semi-intensive culture systems, a combination of fertiliser use and supplemental feeding is common.

Fertilisers used in aquaculture are typically subdivided into two classes: organic and inorganic. The most commonly used organic fertiliser in shrimp and milkfish ponds is chicken manure, dispersed by suspending manure bags in the pond water. If chicken manure is not available, other animal manure from cow, carabao (water buffalo) or pig can also be used. Supplemental doses are regularly added during the culture phase.

Inorganic fertilisers such as a combination of ammonium phosphate (N:P:K 16-20-0) and urea (46-0-0) are applied by the broadcast method in shrimp ponds to enhance growth of natural food. Other inorganic fertilisers used in shrimp ponds are 18-46-0 (diammonium phosphate), 14-14-14 (complete fertiliser), 0-20-0 (solophos), 21-0-0 (ammonium sulphate) and calcium nitrate. Ammonium sulphate is applied during pond preparation not only to enhance plankton growth but also to eradicate pests and predators (Norfolk *et al.*, 1981). In milkfish ponds, the most commonly used inorganic fertilisers are solophos (0-20-0), monoammonium phosphate (16-20-0), diammonium phosphate (18-46-0) and urea (46-0-0).

Although fertilisation can enhance production, it may also cause soil and water conditions to deteriorate if applied indiscriminately.

2.4. Disinfectants

Disinfectants are widely used throughout the world in many spheres of aquaculture. The greatest quantities are used in intensive culture, particularly in finfish and shrimp hatcheries and grow-out facilities. They are used in site and equipment preparation, to maintain hygiene throughout the production cycle and, in some cases, to treat disease. There is little or no use in extensive systems. The classes of compounds listed below are universally available.

Chloramine T (N-chloro-p-toluene sulphonamide)

Widely used for the disinfection of tanks and equipment. Used for the treatment of bacterial gill disease in salmonids, it also has some effect on protozoan ectoparasites on skin and gills. The active component is chlorine (available chlorine = 20%). The disposal precautions discussed below for hypochlorite also apply to Chloramine T.

Formalin

Used as a general disinfectant for equipment. See Section 2.6 for additional environmental and health effects information.

Hypochlorite (Sodium or calcium hypochlorite)

Used world-wide for disinfection of tanks and equipment. The active component is chlorine, which is highly toxic to aquatic life. 96 hr LC_{50} values typically vary between 0.04 and 0.15 mg/l, depending on the species. The chlorine decays with time by the action of sunlight and the consumption of chlorine through its oxidation of organic matter. Many shrimp producers use hypochlorite (or chlorine gas) for viral control, either to disinfect incoming seawater prior to use in hatcheries, or to disinfect water or sediment of the grow-out ponds. Release of chlorinated water to the receiving water body without prior neutralisation with sodium thiosulfate could have localised biological effects. For more information consult Saroglia and Scarano (1983).

Iodophores

Iodophores are a stabilised form of iodine and are used world-wide as disinfectants for aquaculture equipment. They also are used to disinfect fish eggs and are effective against a wide range of bacteria and viruses. It is important that the eggs are not penetrated by the disinfectant. The environmental risk is associated with disposal, which should be to the soil. An example of this class is Povidone.

Ozonation

Used by some shrimp producers to disinfect hatchery water and, less frequently, water in the grow-out ponds.

Quaternary ammonium compounds

Quaternary ammonium compounds (e.g., benzalkonium chloride) are cationic surfactants used as "topical disinfectants" to remove ectoparasites from fish. They have detergent and antibacterial activity and are used widely to treat bacterial, protozoan and monogenean infections. They are also recommended as bactericides and fungicides in shrimp hatcheries. Widely used in shrimp ponds to control infections.

2.5. Antibacterial agents

Antibacterial chemotherapy is applied in aquaculture throughout the world. In many countries there is considerable prophylactic use of antibacterials, particularly in shrimp hatcheries. Bacterial disease occurs most frequently and severely in intensive culture systems and it is there that most antibacterials are used. Antibacterial agents are important in human and veterinary medicine. Thus their use in aquaculture may contribute to increased resistance and cause detrimental effects in medicine more generally. In the USA and in most of Europe use is controlled by drug licensing supported by a surveillance programme to monitor compliance with limits on tissue residues. Since these are relatively new controls, their level of enforcement may vary in different regions, but proper enforcement will be the basis of consumer protection. In other countries, regulations are less restrictive and although some drugs, notably chloramphenicol, are banned, enforcement of such bans is weak or non-existent. Where regulations are lacking or weak, the drug of choice is determined by cost, availability and efficacy.

β-lactams

The benzyl penicillin, amoxycillin (or amoxicillin), has been used for many years in Japan and in the UK since 1990. It may be applied orally in the feed or, less commonly, by injection and has the advantages of reaching maximum tissue levels quickly and rapid elimination; the latter is of benefit if fish are close to harvest. Use is not effective against vibriosis and motile aeromonads are inherently resistant. Because of this and its relatively high cost, it is not widely used. The β-lactams are important in human medicine.

Nitrofurans

Nitrofuran antibacterials, which include furazolidone and nifurpirinol, are a group of synthetic antibacterials. They have antibacterial and antiprotozoal activity and have been used extensively in fish and shrimp farming. Use in Europe and North America has declined as more active compounds have become available and the potential carcinogenicity of the nitrofurans has been appreciated. This has led to their prohibition for use on food animals within the European Union (Samuelsen *et al.*, 1991).

Macrolides

The only macrolide used in fish farming is erythromycin. It is active against Gram-positive bacteria and is used in the control of bacterial kidney disease (*Renibacterium salmoninarum*) and streptococcosis in yellowtail (*Seriola quinqueradiata*) in Japan. It is also used in shrimp hatcheries in Southeast Asia.

"Phenicols"

These are very broad-spectrum antibiotics including chloramphenicol, thiamphenicol, and florphenicol. Use and ingestion of chloramphenicols in humans is associated with aplastic anaemia. There are important uses of the drug in human medicine such as the treatment of typhoid. Chloramphenicol is of genuine concern because, although its use in aquaculture is banned in many countries, its use in others continues. No residue levels are tolerated in Europe and the USA which imposes a control on countries intending to export their products to these areas. Resistance develops readily and is very serious as chloramphenicol is the drug of last resort in human medicine for acute *Salmonella typhi* infection. The major environmental hazard of chloramphenicol is its potential to increase drug resistance.

Two derivatives, the sulphonated thiamphenicol and the fluorinated florphenicol, have been developed for veterinary use and are in use in aquaculture in Japan and some parts of Europe. Available evidence suggests that these are not associated with the adverse effects of chloramphenicol and that resistance develops much less readily.

4-Quinolones

This is a group of synthetic antibacterial agents. The first generation includes nalidixic acid, oxolinic acid and flumequine. The second generation of more potent fluorinated derivatives includes enrofloxacin and sarafloxacin. The former are active mainly against Gram-negative bacteria but the fluoroquinolones have a wider spectrum of activity. Quinolones are widely used in Europe, Japan and other countries in Asia and Latin America. Activity is against DNA metabolism and attempts at repair by the bacterial cell may lead to the generation of resistant mutants. This has occurred readily, perhaps accelerated by the failure to realise that these substances are complexed by divalent cations in seawater where their resultant efficacy is therefore much less than expected. There is some measure of shared resistance among the group. These compounds are resistant to microbial degradation. Photodegradation is possible but not for residues in sediments. (Björklund *et al.*, 1991; Hansen *et al.*, 1992; Samuelsen, 1992; Samuelsen *et al.*, 1992, 1994).

Rifampicin

Limited use of this antibacterial has been reported for treatment of luminous vibriosis in shrimp culture in parts of Southeast Asia (Primavera, 1993).

Sulphonamides

These drugs may be used alone but are more commonly used when potentiated with trimethoprim or ormetoprim. Both the sulphonamides and their potentiators inhibit folic acid metabolism, affecting different steps in the pathway. They are used to control diseases such as furunculosis, enteric red mouth disease, and vibriosis, and are usually applied in the feed. Romet® 30 is an example and one of only two aquaculture antibacterials licensed in the USA. Other preparations are Tribrissen and Co-trimoxazole. Advantages of cost are offset by a tendency to cause product palatability problems. Resistance does develop, but more slowly to the combination than to either component alone. (Samuelsen *et al.*, 1994; Capone *et al.*, 1996).

Tetracyclines

The member of this group in most common use is oxytetracycline, although in some areas chlortetracycline and doxycycline may be used. Oxytetracycline is probably the most widely used antibiotic in aquaculture. It is relatively cheap, can be applied orally or as a bath, and is effective against a wide range of Gram-negative and Gram-positive bacteria such as *Aeromonas* or *Vibrio* spp in fish and crustaceans. Unfortunately, resistance increases readily so that now, in many situations, treatments are ineffective. (Capone *et al.*, 1996; Smith, 1996; numerous other references cited within these papers)

2.6. Therapeutants other than antibacterials

Acriflavine

Occasional use. Acriflavine is a mixture of euflavine and proflavine. Applied as an antibacterial and external protozoan treatment for fish eggs and fry. Potentially mutagenic, as proflavine has been demonstrated to cause mutations in yeast (Albert, 1979).

Copper compounds (Aquatrine®)

Limited use. Effective against external protozoans and filamentous bacterial diseases in post-larval shrimp. It can be used to induce moulting in shrimp as a means of reducing cuticular fouling by filamentous bacteria, and has been employed to treat monogenean infections in fish.

Dimetridazole/Metronidazole

An antiprotozoal agent of very limited use in coastal aquaculture although favoured more strongly by the aquarium trade. Presented as a medicated feed.

Formalin

Aqueous solution of 40% formaldehyde. Global use. Employed as an antifungal agent and in the control of ectoparasites, most often in hatchery systems. Treatment concentrations are typically 15 to 250 µl/l for treatment of fish and crustaceans, and up to 2000 µl/l for control of fungi on eggs. Formalin is toxic to aquatic life at low concentrations, with 96 hr LC50 values ranging from 1 to 1000 µl/l, depending on species (Katz, 1989). Chronic effects are unlikely to occur because of the intermittent nature of treatment and the relatively low persistence of the compound (36 hr half-life; Katz, 1989). To avoid acute effects, however, dilution is necessary in order to insure that therapeutic dosages may be safely discharged to receiving waters. In most current applications, this dilution will occur prior to discharge by mixing formalin-containing effluent with untreated waste streams from other locations on the farm. Formalin is a potential carcinogen and should be handled very carefully to avoid skin contact, eye irritation and inhalation (Katz, 1989).

Glutaraldehyde

Suggested as an alternative to formalin within the European Union but effectiveness is uncertain. Pregnant women should take special precautions to avoid exposure because of teratogenicity.

Hydrogen peroxide

Not in common use. Effectiveness against ectoparasites of fishes is under study.

Levamisole

Very limited use as a medicated feed for treatment of fish nematodes.

Malachite green

Global use as an antifungal and antiprotozoal bath in the culture of shrimp and fish. Principally used in hatcheries rather than grow-out systems. Its use is not permitted in the USA, the European Union and some Southeast Asian countries (e.g., Thailand) due to human health concerns related to its role in respiratory enzyme poisoning. Lengthy withdrawal period essential following application because of persistent residues (see Section 3.8; Alderman, 1985, 1992).

Methylene blue

Occasional use. Effective against fungal and protozoan infections in fish culture operations. May also provide protection against nitrite intoxication.

Niclosamide

Limited use. Applied as an anthelmintic in culture of fish, including turbot.

Potassium permanganate

Occasional use as a bath treatment for fungal infections of milkfish and other cultured finfish.

Trifluralin (Treflan®)

Commonly used prophylactic fungicide; presented as a bath in shrimp hatcheries.

2.7. Pesticides

Ammonia

Widely employed in shrimp culture as a piscicide prior to pond stocking. Anhydrous ammonia or a mixture of calcium hydroxide and ammonium sulphate may be used.

Azinphos ethyl (Gusathion®)

Has been used to remove molluscs from shrimp ponds in the Philippines but its use is now banned.

Carbaryl (Sevin®)

Carbaryl pesticides are used to control burrowing shrimp in shrimp ponds of Central and South America and in on-bottom oyster culture in the north-western USA. The compound degrades rapidly, with reported half-life times at 20°C of a few days (WDF/WDOE, 1985). While active residues remain there can be substantial mortality to non-target species. Non-target crustaceans are likely to be at greatest risk (See Section 3.3).

Dichlorvos (Nuvan®, Aquaguard®)

See entry under organophosphates.

Ivermectin (Ivomec®)

Limited use. Employed to control sea lice in salmon culture grow-out operations in the United Kingdom and Ireland. Residues in marketed fish have been reported from the United Kingdom (MAVIS, 1995).

Nicotine (tobacco dust)

Occasional use. Employed in Southeast Asia as a means to control fish predators and snails during preparation of fish and shrimp grow-out ponds.

Organophosphates

Dichlorvos is a widely used organophosphate pesticide applied to control ectoparasitic crustacean infections in finfish culture. Examples of application include, *inter alia*, salmon culture operations in Scandinavia and the United Kingdom. Concerns have recently been raised with respect to the safety and toxicity of the carrier, di-n-butylphthalate (Burridge and Haya, 1995).

Trichlorfon is also used as an ectoparasiticide in finfish culture, and rapidly degrades to dichlorvos in water. Trichlorfon is the most effective treatment against monogeneans infecting the gills of seabass and sea bream in the Mediterranean.

In addition to dichlorvos and trichlorfon, other organophosphates such as Dipterex®, Dursban®, Demerin® and Malathion® are employed to control ectoparasitic crustaceans in freshwater fish and monogenetic trematode infections in shrimp hatcheries. These compounds may also be applied to eliminate certain parasites and their molluscan and crustacean intermediate hosts. Diazinon® is used in Indonesia for removal of mysids from shrimp ponds.

For all the organophosphates, effects on non-target aquatic organisms, particularly crustaceans is a major concern. Use of organophosphates in agriculture and subsequent run-off of residues into nearby water bodies has been linked to acute effects on indigenous crustaceans (e.g., Kuivala and Foe, 1995). Discharge of pond water containing residues or direct release of organophosphates to waterbodies, for example during lice treatment in salmonid net-cage culture, may result in adverse effects on local organisms (Egidius and Moster, 1987). Due to the high neurotoxicity of organophosphates, potential effects on the health of fishfarm workers are also of concern. (See also numerous references in Alderman *et al.*, 1994).

Organotin compounds (Brestan®, Aquatin®, Thiodan®)

Frequent use in the past in Southeast Asia for elimination of molluscs prior to stocking of shrimp ponds, although banned in the Philippines and Indonesia. Organotin compounds are highly toxic, with acute toxicity to the most sensitive organisms occurring at concentrations in the nanogramme per litre range. For this reason, use of the compounds as antifoulants is severely restricted by Canada, France, Germany, Switzerland, United Kingdom, and the United States. Residues can be found in the sediments near areas of boating activity because of their use in antifoulant paints. Thus, it is possible that acutely toxic residues will remain in pond sediments for months or longer after treatment, although there are no published data on this topic specifically related to pond aquaculture.

Rotenone (derris root)

A compound derived from derris root and used as a piscicide to remove nuisance fish from ponds prior to stocking of shrimp or fish. It presents a hazard to workers as inhalation may result in respiratory paralysis. Use is strictly controlled by many countries.

Saponin (tea seed meal)

Widespread use in Southeast Asia. Employed during the preparatory phase in ponds as a piscicide prior to stocking of shrimps. Also used in the Philippines, Thailand and elsewhere to induce moulting in shrimp.

Trichlorfon (Neguvon®, Dipterex®)

See entry under organophosphates

2.8. Herbicides / Algaecides

Herbicides are widely used to control weed growth in freshwater aquaculture but have very limited applications in marine aquaculture.

Copper compounds (Aquatrine®)

Limited use. Applied to shrimp ponds as a method of algae control.

2.9. Feed additives

The addition of additives to fish and crustacean feeds represents a non-intrusive and, hence, stress-free method by which a variety of absorbable compounds may be delivered to cultured stock. A recent development has been the successful delivery, by dietary incorporation, of artificial and natural pigments, vaccines and immunostimulants, to both fish and crustaceans. Other additives employed by aquaculture feed manufacturers include preservatives, as exemplified by mould inhibitors and antioxidants. The application of live larval foodstuffs as carrier vehicles to deliver a range of therapeutants and alternative (soluble) proteins, while appearing an elegant alternative to other treatment methods, has met with equivocal success. There are no data on environmental or health effects specific to aquaculture, though many of these compounds are widely used as feed additives in terrestrial animal husbandry.

Astaxanthin

Widely used in north-western Europe and North America, particularly for the artificial coloration of the flesh of salmonids during the latter stages of grow-out operations.

Butylated hydroxyanisole

Used in South and Southeast Asia as an aquaculture feed preservative due to its antioxidant properties.

Butylated hydroxytoluene

Widely used as an antioxidant in aquaculture feedstuffs. While the pure chemical has toxicological effects at excessively high levels of exposure, the concentrations used in feeds would be below this threshold.

Canthaxanthin

Widespread use in North America and north-western Europe, particularly for the artificial coloration of the flesh of salmonids during the latter stages of grow-out operations.

Carotenoids

See astaxanthin and canthaxanthin.

Ethoxyquin

Widely used as an antioxidant in aquafeeds.

Feeding attractants

Limited use as a 'start-feeding' stimulant for marine fish, abalone and shrimp larvae.

Immunostimulants (e.g., b-1,3-glucans, peptidoglycans)

Limited use globally, but increasing. Used to stimulate the non-specific immune system of shrimps and finfish.

Vitamin C (ascorbic acid)

Widespread use. Reported to enhance disease resistance and to prevent deficiency syndromes in fish, including lordosis, scoliosis and petechial haemorrhaging. Tiger shrimp with ascorbic acid deficiency show moulting incompetence, malformation of carapace, disorder of the gill and associated high mortality. Used during all stages of the production cycles of salmonids, yellowtail, milkfish, seabass and for juvenile stages in tiger shrimp production. Also provided as a feed supplement to shrimp where algal production of ascorbic acid within ponds is inadequate.

Vitamin E

Widespread use. Reported to enhance disease resistance although contradictory evidence is available (e.g., Lall *et al.*, 1988; Hardie *et al.*, 1990). Dietary addition prevents deficiency syndromes, including muscular dystrophy, anaemia and oxidative damage to cell membranes. Used during all stages of the production cycles of salmonids, yellowtail, milkfish, seabass and tiger shrimp.

2.10. Anaesthetics

A number of anaesthetic agents have been used in aquaculture to assist immobilisation of brood animals during egg and milt stripping. Anaesthetics are also extensively used to sedate and calm animals during transportation. This is particularly true for seed fish, although anaesthetics and sedatives have also been used during transport of broodstock. In high value individuals, both sedatives and anaesthetics are used for treatment purposes (topical, injections, etc.). Anaesthetics are fundamentally employed at very low doses, such that their limited use in coastal aquaculture presents no significant environmental risk although there may be hazards to users.

Benzocaine

Widespread use. Applied during egg and milt stripping and for transportation purposes. Clearance rates are rapid.

Carbon dioxide

Used as a general sedative.

Metomidate

Not widely employed due to high cost but has been reported to be an effective agent to calm brood stock (e.g., salmonids) in Canada.

2-phenoxyethanol

Minor use globally. Mainly employed during egg and milt stripping. Potential effects on human health, including development of rashes, limit its use.

Quinaldine

Common usage. Employed for the transport and handling of fish.

Tricaine methanesulphonate (MS222)

Used world-wide and registered for use with fish in the USA. Used in stripping eggs of salmonids and other species as an anaesthetic at low dosages, but the margin between anaesthetising and acutely toxic concentrations is small. Low persistence in the aquatic environment.

2.11. Hormones

Carp pituitary extracts, semi-purified, and purified hormonal preparations, together with synthetic peptides and their analogues, play an important role in the aquaculture industry. For example, the ability to control and or induce ovulation laid the foundation for total control of life cycles in many species, thus ensuring uninterrupted supply of eggs and fry, while enabling hybridisation. More recent innovations in the application of hormones to aquaculture include teleost sex control (reversal) measures, thereby supplying so-called "monosex" lines which exhibit enhanced production characteristics. The advent of recombinant DNA technologies has provided an array of other potentially useful preparations. While some, such as somatotropin, are undergoing commercial testing, others await further evaluation.

Growth hormone (GH, somatotropin)

Limited use. A recombinant natural trout GH preparation has recently been successfully field tested as a smolt enhancing agent in salmon culture. A number of sustained release formulations have also been field tested and show good potential for growth acceleration and enhanced feed conversion efficiency during the grow-out phase of salmonids. At present, 17 countries have cleared GH preparations for agricultural use (IFST, 1996).

17a-methyltestosterone

Widespread use as an androgenic agent in masculinisation of salmonids, tilapia etc. Usually incorporated in the diet of fry prior to sexual differentiation.

Oestradiol 17b; ((17b)-estra-1,3,5(10)-triene-3,17-diol; 17b-estradiol)

Broad use both experimentally and commercially (Satoh *et al.* 1992; Blazquez *et al.* 1993), as a means of controlling sex in cultured teleosts. Delivered in feed to larval and juvenile stages. May reasonably be assumed to be carcinogenic, since a number of estrogenic agents, including 17b-estradiol, have been shown to stimulate growth of human prostate cancer cell lines (Castagnetta and Carruba, 1995), and are potent tumour promoters, by direct or indirect action, in hepatic and renal tissues of rodents (Zhu *et al.*, 1993; Lupulescu, 1993; Ni and Yeager, 1994). Recent evidence also indicates that 17b-estradiol may enhance tumorigenic actions of dehydroepiandrosterone in trout (Orner *et al.*, 1996).

Ovulation-inducing drugs

Includes a wide range of crude, semi-purified, purified and synthetic products. Examples include carp pituitary extracts (crude, lyophilised etc.), partially purified gonadotropins (e.g., SG-G100), human chorionic gonadotropin, GnRH and analogues, etc. In certain instances, induction of spawning requires the use of a dopamine agonist, the most common in use being domperidone. World-wide use to control reproduction in fishes. Delivered by injection, through injectable pellet or orally. As these chemicals are only used in broodstock they do not enter the human food chain and are of no environmental significance.

Serotonin (3-(2-aminoethyl)-1H-indol-5-ol; 5-hydroxytryptamine; enteramine; thrombocytin)

Limited use, delivered by injection. Has been employed successfully, combined with temperature shock, for the artificial induction of spawning in giant clams in enhancement facilities in Indonesia, the South-Pacific islands and Australia.

All of the chemicals listed above can be classified as endocrine disruptors and, indeed, are used for this purpose. Although the potential human health and environmental effects of endocrine disrupting chemicals is now a matter of considerable debate (Colborn *et al.*, 1993), the use of such chemicals in aquaculture is not currently a major concern. Hormones used to induce ovulation usually would be administered by injection (thus minimising environmental release), and are given only to broodstock which are not to be used for human consumption. Hormones used for sex control in fishes (testosterone and oestradiol) are administered through the diet, but are only given to fry. Thus, the biomass treated (and amount of hormone needed) is minimal and a year or more will normally elapse before the fish are harvested. Use of growth hormones in aquaculture remains experimental but is becoming increasingly widespread in other areas of animal production.

3. ISSUES OF CONCERN

The primary environmental and human health issues associated with chemical use in coastal aquaculture are described below. The order is not meant to imply any ranking of priority.

3.1. Persistence in aquatic environments

Many aquaculture chemicals degrade rapidly in aquatic systems. For example, formalin, a widely used parasiticide and fungicide, has a half-life in water of 36 hours (Katz, 1989). Furazolidone, an antibacterial, has a half-life in sediments of less than one day (Samuelsen *et al.*, 1991). The half-life of dichlorvos, a parasiticide, in seawater is in the range of 100-200 h, depending upon water pH (Samuelsen, 1987).

Other chemicals may persist for many months, retaining their biocidal properties. Metal-based compounds, such as the organotin molluscicides and copper-based algaecides are likely to be quite persistent in aquatic sediments, although precise data are lacking. Some antibacterials, notably oxytetracycline, oxolinic acid and flumequine, can be found in sediments at least 6 months following treatment (Weston, 1996).

Clearly, the persistence of chemical residues is highly dependent on the matrix and ambient environmental conditions. In general, residues in water are less likely to be of long-term concern because of photodegradation and dilution to below biologically significant concentrations. Residues incorporated into sediments tend to persist for longer periods, particularly if the sediments are anaerobic as may be expected under fish cages. Very little is known about the environmental fate of many aquaculture drugs with available data being derived largely from temperate latitudes. Persistence in tropical environments is poorly studied and may be different due to soil characteristics or temperature-dependent microbial activity.

3.2. Residues in non-cultured organisms

Use of pesticides, antibacterials and other therapeutants in coastal aquaculture has the potential to result in chemical residues appearing in wild fauna of the local environment. For example, uningested medicated feeds or faeces containing drug residues provide routes by which local fauna may ingest and incorporate medicants. Among the fauna prevalent around aquaculture operations that seek food or take advantage of shelter and ecological niches created by structures, the filter-feeding molluscs in down-current areas are particularly vulnerable to "secondary medication" from contaminated particulates. Such inadvertent chemical exposures and subsequent human consumption of aquacultural products can present hazards to human health. This is most likely in the case of systems practising polyculture or when two or more aquaculture facilities interact. Limited data with oxytetracycline have failed to substantiate this concern (Capone *et al.*, 1996) but mussels near net-cages have been found to contain oxolinic acid (Ervik *et al.*, 1994). Sport and commercial fishermen, including fish farmers, may also take advantage of the enhanced density of fish and shellfish in the vicinity of aquaculture facilities and this may result in increased human exposures to residues. A number of studies have been published which demonstrate that oxolinic acid residues in a range of wild fish and shellfish around a salmon net cage site can persist for one to two weeks after cessation of chemotherapy in the cages (Samuelsen *et al.*, 1992, Ervik *et al.*, 1994). Similar results have been reported for oxytetracycline (Björklund *et al.*, 1991, Capone *et al.*, 1996).

3.3. Toxicity to non-target species

Toxicological effects on non-target species may be associated with the use of chemical bath treatments, pesticides, disinfectants, or leaching of toxicants from antifouling chemicals employed in aquaculture. Among the pesticides that may have toxicological effects on the surrounding invertebrate fauna are the organophosphate ectoparasiticides, such as those employed in salmon culture in many parts of the world. Organophosphate (OP) bath treatments result in the release into the surrounding waters of significant quantities of toxic material liable to affect crustaceans, particularly larval stages (Egidius and Moster, 1987). The use of carbaryl pesticides to eliminate burrowing shrimp from oyster beds in the north-western United States results in the unintended mortality of Dungeness crab, a commercially exploited species (WDF/WDOE, 1985).

3.4. Stimulation of resistance

Since the first true antibacterial agents were introduced in the 1930s, users have been coping with the emergence of drug resistance among target organisms. As each new drug was developed, major successes in therapy were achieved but, within a few years, the first cases of drug resistant strains began to appear. The best documented cases are in human medicine. Before continuing to consider the ways in which resistance in bacteria may result from the use of chemicals in aquaculture, it is necessary to define what is meant by resistance. To be susceptible to the effects of any antibacterial, an organism must possess a target system that is affected by the presence of the antibacterial agent. Bacteria which lack such target systems are inherently resistant. Bacteria which normally have susceptible target systems may become resistant to the antibacterial by a range of modifications, either to the target system itself, e.g. a bacterial ribosome, or by a change in cell wall permeability resulting in decreased access of the drug to the cell. Alternatively, bacteria may produce new enzymes, e.g. β-lactams which act directly on the drug and cause inactivation.

Bacterial resistance may be acquired either by the acquisition of foreign DNA or by modification of chromosomal DNA. This may result in mechanisms by which drug entry to the cell is blocked, the drug is inactivated, or the affinity of the target site is altered, or cellular dependence upon the blocked pathway is reduced (Cooksey, 1991). The origin of resistance is much older than current antibacterial chemotherapy. Microbial species such as *Streptomyces* (Levy, 1989), which produce antibiotics, carry resistance genes and it is postulated that resistance may have spread outwards from such sources. DNA then may be transferred between bacteria by a variety of routes including plasmids, conjugative transposons and bacteriophages as well as by free DNA (Chopra, 1985). Plasmids are genetic elements that are independent of the chromosome. Some are capable of becoming inserted into the chromosome and are able to exist either in a chromosomal state or in a plasmid state. In the plasmid state they can mediate resistance transfer at high frequency within and between bacterial species and may result in the transfer of resistance to two, three, four or more antibacterials simultaneously. The incidence of R-plasmid transfer associated with aquaculture has been reviewed by Aoki (1992).

Alternatively, resistance may result as a direct consequence of the antibacterial as in the case of resistance to the quinolones (Lewin *et al.*, 1990). Because the quinolones affect the replication of bacterial chromosomes through their effect on bacterial DNA gyrase, resistance cannot be plasmid mediated because plasmid replication is prevented. Instead, quinolone resistant bacterial strains either have mutational changes in their DNA gyrase resulting in resistance, or they have mutational changes in the cell wall which prevent entry. However, laboratory studies have shown that culture of bacteria in the absence of a drug favours the selection of sensitive variants and under these conditions the proportion of resistant variants declines (Lee and Edlin, 1985, Modi *et al.*, 1991). Under the positive selection pressure of drug use, resistant variants increase in relative proportion, further transfer is encouraged and resistance is expressed. When a drug is withdrawn, the incidence of resistance may recede but is unlikely to disappear.

In intensive aquaculture, antibacterial agents are used universally to treat bacterial disease and there is widespread prophylactic use (Inglis, in press). The most common routes of application are oral or by immersion. In both cases, significant quantities of antibacterial may reach the environment and lead to the selection of resistance. This has resulted in increased resistance both in obligate fish pathogens such as *Aeromonas salmonicida* and in the opportunistic pathogens such as *Vibrio* spp. and the motile aeromonads (Aoki *et al.*, 1984; Zhao *et al*, 1992). It is theoretically possible for non-pathogenic bacteria in the marine environment to transfer resistance to human pathogens by plasmid transfer although it has been argued that such a scenario is unlikely (Smith *et al.*, 1994a).

Factors affecting the success of chemotherapy have been more widely studied than environmental aspects. Risk factors predisposing to resistance selection amongst pathogens are beginning to be identified. In general terms, it is agreed that antibacterial resistance is associated with, among other things, the frequency of antibacterial use in an environment. Studies in human and veterinary medicine support this (Prescott and Baggott, 1988; Hamilton-Miller, 1990; Kruse, 1994) and it is reasonable to assume that similar factors pertain to aquaculture. There are many reports of resistance in collections of fish bacterial pathogens and some reports from diagnostic laboratories of resistance trends that provide strong inferential, but not definitive, evidence of a causal link with antibacterial use in aquaculture (Sangrungruang *et al.*, 1995; Tsoumas *et al.*, 1986; Inglis *et al*, 1991; Meier *et al.*, 1992).

The frequency of resistance would also be increased by the presence of antibacterial agents in concentrations that are insufficient to kill the bacteria. This situation might arise because of:

- Wrong choice of drug, i.e., failure to recognise the need for a rapid initiation of treatment and for adequate laboratory support, including the characterisation of resistance (Smith *et al.*, 1994a).

- Failure to deliver an adequate dose. This may be due to the inappetence of the fish, leaching losses before the feed reaches the target (Inglis *et al.*, 1993) or low drug bioavailability.

- Faulty treatment regimes. Achievable tissue levels associated with different treatment regimes are poorly understood - some may deliver only sub-bactericidal levels of a drug. Duration of therapy is also very important. Although gross symptoms may disappear quickly, the pathogen may persist in the host. Failure to complete a course of treatment presents a strong selection pressure for resistance to emerge within the host.

- Using antibacterials for prophylactic treatment can provide a strong selective pressure for resistance.

- Heavy reliance on a very limited number of antibacterials, either because of regulatory limitations or the aquaculturist's preferences for therapeutants.

Resistant opportunistic bacterial pathogens may enter the environment as a result of treatment failures. Bacteria in the aquatic environment are affected more directly by drugs in uneaten feed or by leached, unabsorbed or excreted drug. Most relevant studies have been carried out in northern Europe, particularly Norway. Elevated levels of resistance have been reported that are associated with persistence of oxolinic acid and oxytetracycline around salmon cages (Björklund *et al.*, 1991; Samuelsen, 1992). In another study, resistance in culturable environmental bacteria was shown to rise from 1% to 8% to oxytetracycline and between 1% and 12% to a potentiated sulphonamide (Herwig *et al.*, 1997). Resistance declined over the succeeding two months after the cessation of drug use. Similarly, in a study in Ireland, oxytetracycline in the sediment was associated with an increased incidence of resistance which was lost after one to two months (Kerry *et al.*, 1995). It is not known whether the results of these studies reflect the emergence of true resistant bacterial strains or simply a shift in the bacterial population allowing intrinsically resistant bacteria to increase in numbers because of reduced competition. Unless the "resistant" cells can be identified (a major task not so far addressed in any published study), it remains most likely that a change in species composition has been achieved with inherently resistant species replacing the susceptible ones. As the effects of the antibacterial therapy disappear, the normal structure of the local bacterial flora gradually recovers. This is not, strictly speaking, a pattern of "selection for drug resistance" because it is likely to involve inter-specific rather than intra-specific mechanisms. It should be noted that the appearance of an antibacterial-resistant bacterial assemblage near aquaculture facilities is not always associated with the use of antibacterials at the site, indicating that there are confounding factors in measuring antibacterial resistance (Smith *et al.*, 1994a).

3.5. Effects on sediment biogeochemistry

The microbial communities of aquatic sediments degrade organic matter and recycle associated nutrients. Rates of oxygen consumption, ammonium and sulphide production in sediments are all highly dependent upon microbial activity. Accumulation of antibacterial residues in sediments has the potential to inhibit microbial activity and to reduce the rate of organic matter degradation.

Only two studies have examined this issue. Capone *et al.* (1996) found oxytetracycline residues up to 7 mg/kg in the sediment had no effect on microbial density or activity although information regarding possible shifts in community ecology was not examined. Conversely, Hansen *et al.* (1992) found 40-50% reduction in microbial density and a >90% decrease in activity (as measured by sulphate reduction rates) with the addition of 100-400 mg/kg of oxytetracycline, oxolinic acid and flumequine. Thus, the potential inhibition of microbial density and activity appears, not surprisingly, to be very dependent upon the concentrations of antibacterial residues. Effects are likely to be even more dramatic as salinity decreases and the bioavailability of these drugs increases.

If antibacterial residues were to slow the rate at which organic matter is degraded, there could be adverse consequences to farm production. Pond management techniques generally strive to encourage aerobic decomposition of organic matter, as this results in the production of low-toxicity products such as carbon dioxide and nitrates. Anaerobic degradation yields more toxic products such as sulphides and ammonia. If the presence of antibacterial residues reduced the extent of aerobic degradation of organic matter, more organic carbon would be incorporated into the anaerobic portion of the sediment column. Subsequent anaerobic degradation could result in an increased production of toxic end-products. Such a scenario is entirely speculative but it illustrates the need for more information on the consequences of the use of antibacterial agents on sediment geochemistry.

3.6. Nutrient enrichment

Fertilisers are often used in pond culture operations to increase primary productivity. If hypernutrified waters are discharged in the effluent, they could have similar effects in receiving waters, especially when the latter are nutrient limited. The nutrient input associated with the use of fertilisers could be additional to the contributions of feed in systems employing both feed and fertilisation. Whether these nutrient inputs are of significant ecological consequence depends on local conditions. Some tropical reefs are particularly susceptible to eutrophication. Conversely, studies at temperate latitude salmonid farms have found that hypernutrified waters are dispersed before the additional nutrients can be converted to local phytoplankton biomass thereby resulting in no measurable eutrophication (ICES, 1994).

3.7. Health of farm workers

There is potential for some chemical compounds used in coastal aquaculture to pose health risks to site workers. Accordingly, proper training and the provision of adequate safety equipment is essential. Some chemicals, such as the organophosphates (dichlorvos and trichlorfon) and others that act as respiratory enzyme poisons (malachite green) must be handled with respect, especially in concentrated form. Rotenone in powder form is toxic by inhalation and may cause respiratory paralysis. Other compounds, such as hydrogen peroxide, now being introduced in some areas to replace organophosphates as ectoparasite treatments, present major problems in handling and transport because of their explosive nature.

With antibacterial agents, the principal human health risks are associated with hypersensitivity reactions. Giroud (1992) concluded that although risks existed, there was no evidence that actual harm had occurred and that with recognition of the hazards and the tighter health and safety controls currently being imposed in most countries, the risks are probably more theoretical than actual. However, when medicated feeds are prepared on farm sites, often using simple techniques such as manually mixing active compounds, or a medicated premix, with feed before adding oil to attach the drug to the feed, considerable dust hazards may be encountered. Without adequate protection, workers may be exposed to the hazards of dust containing sufficient drug to produce hypersensitivity reactions.

If proper health and safety precautions for handling aquacultural compounds presenting significant health risk to humans are enforced, operator risk will be minimised. Particular care must be exercised with regard to pregnant women, because of the teratogenic properties of some compounds. Whenever chemicals are used in aquaculture it is essential that both employer and employee consider the risks associated with their applications.

3.8. Residues in seafood

Perceptions regarding the hazards of chemical residues in aquacultural products are an increasing source of anxiety among consumers. Although most areas of aquaculture, particularly those which employ low density production methods, use few or no chemicals that could give rise to persistent residues in the flesh of the products, these perceptions unfortunately affect the entire industry. Increasingly, developed countries are imposing restrictions on compounds used by their own fish farmers and introducing residue monitoring programmes for imports. Such monitoring programmes will also be required of producing countries who wish to continue exporting their aquaculture products into international markets.

When an animal is treated, either by bath, oral or injection routes, with any chemical for therapeutic or other purposes (e.g., anaesthesia), the chemical will generally be absorbed by the animal concerned. For example, a 1 mg/l bath of malachite green (topical fungicide/parasiticide) for 1 hour can produce a blood serum level in fish of up to 14 mg/kg at temperate water temperatures. Its elimination (excretion) from fish tissues is extremely slow - in excess of 2000 degree days (e.g., 200 days at 10°C) are required for the residues of one treatment to be eliminated (Alderman and Clifton-Hadley, 1993). Although other chemicals present less spectacular examples, many have post-treatment residues that may persist for days to weeks.

With the increasing development of technology, methods for detecting drug residues in animal tissues continue to increase in sensitivity. The concept that animal tissues should be totally free of all detectable residues has become unrealistic because it depends on the analytical method employed, many of which are of much enhanced sensitivity relative to older methods. For this reason, the concept of the maximum residue limit (MRL[1]) has been introduced and used by food safety experts. The MRL is the maximum concentration of residue resulting from the use of a drug that is recognised as acceptable in food. It is based on the amount of residue considered to be without any significant toxicological risk for human health.

In order to ensure that no residues above MRL are present in the edible tissues of aquaculture products, a withdrawal period must be introduced following treatment (i.e., a time delay that must be imposed between cessation of therapy and harvesting). With well-established veterinary medicines this will often be indicated on the label of the product itself. However, in aquaculture products, most research on this topic has been carried out in temperate climates and on temperate species. For example, information regarding withdrawal times in salmonid production may be of little value in establishing appropriate withdrawal times in tropical shrimp culture. Both fish and shrimp are poikilothermic animals (i.e., their body temperature and therefore their metabolic rate is largely determined by water temperature). It is therefore reasonable, as a first hypothesis, to presume that recommendations pertaining to temperate climates are likely to be conservative approximations of appropriate tropical withdrawal periods. However, the difference between marine tropical fish species and the even greater potential metabolic differences between fish and crustaceans mean that such approximations will need to be supported by new experimental data. Thus, better information on uptake, distribution and elimination rates (pharmacokinetics) for the major drug groups is needed. Results from such studies are now beginning to appear (Mohney *et al.*, 1997). Pharmacokinetic studies should also consider the health status of the fish as very different availability and excretion dynamics have been reported by Uno (1996) for oxytetracycline among *Vibrio*-infected and unaffected ayu (*Plecoglossus altivelis*).

Concern for the presence of residues is associated with possible effects on consumer health, either in the form of immediate hypersensitivity reactions, such as may occur in people sensitised to β-lactam antibiotics, with possible effects on gut flora from low levels of antibacterials that might select for resistance and with potential toxicological effects. The protection of consumers against the risks of ingesting veterinary medicines is receiving much attention (Corpet, 1992; Yndestad, 1992). Although these risks may be difficult to quantify, it is essential that aquaculture products conform to standards no less protective than those already in place for many other areas of animal production.

4. PROBLEMS AND SOLUTIONS

4.1. Intensification, fish health management and access to information

Although the majority of aquaculture operations are still based on extensive and semi-intensive farming systems, there is a trend in many regions of the world to intensify aquaculture practices to enhance yields and to improve the efficiency of the production process. In many cases, aquaculturists are learning quickly to use available resources more efficiently, for example through improved management of water resources and water quality, by opting for better quality seed, optimising stocking densities of seed fish, refining feeding techniques or using more appropriate feeds and/or fertilisers. Design and engineering of farming facilities, use of equipment, and preparation, maintenance and operation of farming units are being improved. In addition, more suitable sites are being selected when new operations are being started. Improved usage of chemicals is often contributing to enhanced production efficiency as well as to reduction of wastes and losses.

However, many aquaculturists are facing problems resulting from unsuccessful farm management, from incidences of diseases and/or disease epidemics, or from increasing contamination of their intake water supplies. Some aquaculturists, in attempting to intensify their production process, have exceeded the capacity of their farming system. For example, production

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[1] MRLs are generated by a number of bodies such as the European Union and more globally within the framework of the FAO/WHO Codex Alimentarius Commission, which is advised scientifically by JECFA (Joint FAO/WHO Expert Committee on Food Additives). Often the scientific information evaluated by these bodies is the same and some experts who form part of the national and market area residues committees are also members of JECFA. Thus, for the most part, MRLs from the different bodies tend to be identical or very similar. The calculation of any MRL is complex and cannot be considered in detail here. Briefly, is calculated from an ADI (acceptable daily intake) which, with safety factors, is itself based on an NOAEL (no observable adverse effects level) derived from animal and *in vitro* trials.

losses have occurred due to practices of over-stocking, inadequate management of water quality and water supply, and over-feeding. In many cases, phased development and a gradual process of intensification would help to avoid farm collapses that may occur when production is increased too quickly. Usually much practical experience is required to establish the limits to intensification in aquaculture farming systems, given their complexity and the diversity of species cultured. Frequently, it is the aquaculturists who are in the best position to understand and manage the complex biological, chemical and physical interactions prevailing in their farming units. Some aquaculturists have experienced serious difficulties in managing the consequences of inadequate measures or excessive application of inputs into their farming system, when pursuing increased production yields. Unfortunately, disease outbreaks often result from management deficiencies.

Disease outbreaks can be a very serious threat to the cultured stock, and aquaculturists often do not have, or do not see, any alternative to the application of disease control chemicals to treat or prevent such outbreaks. The livelihoods of many aquaculturists, particularly in developing countries, depend on the successful grow-out of their stock. It is often the fear of disease outbreaks, or desperation when an outbreak has occurred, which leads to the use or misuse of disease control chemicals. A key problem is a lack of sufficient knowledge and experience of appropriate aquatic health management measures. The management practices necessary to maintain farm resources, such as water and feed, and to maintain good health conditions are sometimes poorly understood. In addition, basic fish health management measures aimed at preventing and reducing risks of disease outbreaks are often not known.

In most cases, aquaculturists do not have access to sufficient information, such as the appropriate method of use, dose, efficacy, target organisms, potential for adverse effects, and withdrawal periods, regarding disease control chemicals. For example, chemicals are sometimes sold with inconsistent concentrations of drug ingredients or mixtures of different drugs. Even if the relevant information is provided on labels, such chemicals may have been "repackaged", leading the aquaculture farmer to believe that he/she has bought a high quality product of guaranteed efficacy and safety. Consequently, there is an obvious need for guidance on safe and effective use of disease control chemicals in hatchery and farm operations.

Technical guidance on chemical use should be provided by experts in aquatic animal health management. Fortunately, there is an increasing number of fish disease specialists with experience regarding the species cultured and aquaculture farming systems used, who can advise on appropriate farm management measures and, if necessary, on the choice of the most suitable chemicals to treat diseases effectively. However, it appears that provision and dissemination of information on safe and effective use of chemicals through education, training and extension should not be limited only to hatchery and farm operators. Manufacturers of drugs or medicated feeds and "middlemen", such as traders, suppliers and retailers (salesmen), have an important role in exchanging and disseminating information on safe and effective use of chemicals in aquaculture.

There is a need to enhance public awareness and understanding of the use of chemicals in aquaculture. In many countries, there is insufficient understanding of the diversity of aquaculture farming practices and of the chemicals being applied in hatcheries and grow-out units. The general public, especially the consumers of aquaculture products, are often unaware of the benefits and advantages of chemical use in aquaculture. Neither is it sufficiently appreciated that many chemicals used in aquaculture present insignificant risks to humans or the environment. Nevertheless, marketability and consumer acceptance of aquaculture products may be affected if there is a perception that aquaculture products have been produced using hazardous chemicals. In some countries, misconceptions about chemical use in aquaculture are being enhanced by pressure groups through statements which often are unsupported by scientific evidence or conceived without adequate knowledge of aquaculture practices. Fortunately, an increasing number of aquaculturists are aware of the risks that may stem from the use of chemicals that can cause detrimental effects in humans and the environment or from the misapplication of chemicals considered safe when used properly.

4.2. Residues, methods and enforcement

The problem of residues of chemotherapeutants in edible tissues of aquaculture products is now attracting world-wide attention, particularly among those charged with maintaining food safety. Many developed countries (e.g., the European Union, USA, Japan, Canada, New Zealand, Australia) screen domestically-produced and/or imported seafood to ensure that chemotherapeutant levels are below the requisite Maximum Residue Limits (MRLs). There are considerable problems, however, with such screening programmes. First, the analytical costs can be quite high, perhaps up to US$ 300 per analyte per sample. Second, standard analytical methods for many chemotherapeutants simply do not exist. For example, no methods are available for the detection of residues of furazolidone and other nitrofurans in tissues. The USA has, until recently, screened salmon only for oxolinic acid and shrimp only for chloramphenicol (Weston, 1996). Many other chemotherapeutants are in widespread use but their residues would go undetected.

One solution to these problems, at least for the antibacterials, is adoption of microbiological rather than chemical (typically HPLC) assays. While the microbiological methods are less sensitive and do not differentiate among different drugs, they do establish if the tissue being tested contains antimicrobial residues. An optimal screening programme would involve analysis of a large number of samples by microbiological methods, followed by chemical confirmation and identification of residues in those samples testing positive. However, microbiological methods only detect bioavailable (i.e., biologically active) antibacterials, while chemical methods can also detect residues that are not in a biologically active form (Alderman *et al.*, 1994).

An overriding problem in any residue screening programme is the sheer magnitude of commerce in aquaculture products. Most import monitoring programmes analyse, at most, one sample per 100 tonnes. Such a level of screening is not adequate to ensure that seafood containing residues above MRLs does not reach consumers. At best, this screening will identify suppliers whose products consistently fail to meet residue standards.

Perhaps the best approach to controlling residues is the maintenance of quality assurance protocols (including residue screening) by producers, either under the aegis of governments or a trade association. It may be anticipated that commercial pressures and more stringent controls imposed by importing countries are likely to force exporters to meet the quality standards of their primary markets (See further discussion under 4.7). However, the introduction of residue monitoring standards may pose a dilemma for developing countries exporting aquaculture products - how to meet the requirements of the importing countries and how to fund the necessary programmes? One risk of tightened export residue controls is that products that fail to meet standards may be released to domestic markets. Shrimp sold during 1990-91 in domestic markets in Bangkok have shown an annual average of 8% of the samples with measurable oxytetracycline and oxolinic acid residues and a maximum of 37% in any one sampling event (Saitanu *et al.*, 1994).

4.3. Prophylactic use of antibacterials

Prophylactic use of antibacterials (i.e., the use of these drugs to prevent rather than to treat disease) continues to be widespread in some aquaculture sectors. The practice of providing antibacterial protection for Atlantic salmon smolts in Europe immediately before their transfer to sea has been largely discontinued because effective vaccines have become available. In other sectors, such as both shrimp and some fish hatcheries, prophylaxis is common and applied to prevent bacterial and fungal diseases. Chloramphenicol and oxytetracycline are used in the former case and trifuralin in the latter. Problems associated with this practice include the "banned" status of chloramphenicol (see Section 4.7.), the general selective pressure for resistance due to frequent use of broad spectrum antibacterials outside of a defined therapeutic regimen and the cost of procedures that largely have become ineffective.

When the pathogen can be specifically defined, vaccination or use of pathogen-free broodstock, eggs and systems can be effective. Vaccination of salmon smolts against furunculosis is now proving successful in Europe and North America. Certification schemes for stock and eggs free of *Renibacterium salmoninarum* (bacterial kidney disease of salmonids) and of *Cytophaga psychrophila* (rainbow trout fry anaemia syndrome) operate in the USA and Europe. This solution is not directly applicable to warm water diseases such as those due to vibriosis and motile aeromonads where many species which are widespread in the environment are involved. Vaccine development in shrimp is hindered by poor understanding of the immune system. The immunological memory is short in these crustaceans so that even an effective vaccine may not offer cost-effective solutions. Research in shrimp immunology is an active field and the results of relevant studies should be considered.

The most promising approach in shrimp culture appears to be production of better quality postlarvae for pond release. Studies by Pitogo (unpublished) have shown that it is the smaller postlarvae which are most likely to suffer vibriosis. Good nutrition is seen as central, with diets optimised for the levels of vitamins, fatty acids and minerals. The addition of immunostimulants to feed appears promising in enhancing general resistance to microbial diseases in shrimp. This practice has been effective in fish culture but understanding of dosage, duration of treatment and length of stimulation is still incomplete. Many products are being introduced to the market and there is a need for further systematic evaluation, particularly in relation to shrimp culture.

Shrimp production in hatcheries can be a capital intensive industry and farmers regard postlarval survival rates as critical to their economic viability. High stocking levels are essential to provide an adequate return on invested capital. It is likely, therefore, that hatchery operators would be amenable to the introduction of new practices if they offered good prospects of success. Prophylactic use of antibacterials is heavily concentrated in this sector and future work to optimise health management and nutrition appears to be the best way forward.

4.4. Quality assurance of chemicals used in aquaculture

Chemicals used in aquaculture, particularly those directly aimed at disease control, should be labelled with accurate information on the concentration of the active ingredient(s). Labels should also carry information on recommended use in the aquaculture sector for which the product is intended including :

- geographic region
- fresh, brackish or seawater environment
- species cultured and life stage
- route/mode of treatment
- withdrawal period (with reference to species and temperature)
- potential hazards to environment and human health (including treatment in case of accidental ingestion or contact).
- storage requirements and expiry date
- disposal methods for unused product

Such information should be included in local language(s). Large international pharmaceutical companies are increasingly providing much of this information but data specific to tropical environments and species is often incomplete or absent. Smaller producers seldom have the laboratory support to generate such information. Re-packaging is widespread in Asia and may occur elsewhere. In such cases, label information is rarely passed on with the new packaging and, furthermore, the product may have been adulterated, diluted or "improved". This presents a problem to the farmer trying to follow a recommended treatment regime and may have implications in relation to antibacterial agents.

The solution is to provide comprehensive forms of labelling. Ultimately, responsibility rests with the chemical producer but traders and sales promotion personnel must ensure that this is passed on, that the product is not altered and that claims are not made beyond those which can reasonably be supported by the chemical producer. Major companies, in the main, comply, although there is a need for them to generate more data relevant to the aquacultural application of their product in specific situations. This co-operation should be sought. More difficulty may be anticipated with small 'own-brand' producers who are unlikely to take action unless they can see commercial advantage. The same applies to re-packagers who are already exploiting the situation.

Joint endeavours by government agencies, trade associations and training establishments could improve the current situation. Government agencies in many countries assume responsibility for setting up registration schemes for hazardous chemicals and medicines. Even those countries that do not specifically approve chemicals for aquaculture often ban the use of some specific compounds. However, there is sometimes no effective way of enforcing government policy and fines are too light to deter violators. A more productive approach may be for government authorities or trade associations to develop a certification system. Satisfactory products given a seal of approval by recognised authorities would have commercial advantage, thereby justifying the cost and effort involved. Trade associations could compile a 'black list' of products which, according to information that they receive from members, have consistently failed to perform as claimed. Strong farm co-operatives have the potential for bulk buying and thereby the ability to influence suppliers. Such associations of aquaculturists do exist in Europe, the United States and Asia. They constitute an option for improving the service from suppliers to the aquaculture industry.

4.5. Need for data on quantities of chemicals used

Efforts to evaluate the risks of chemical use are hindered by the lack of quantitative data on the amounts of chemicals used. At best, only the fact of use is known and individuals with knowledge of industry practices may be able to qualitatively describe the use of a given agent as "negligible", "common", "widespread", etc. The only country for which quantitative data are available is Norway. These indicate that the amounts of antibiotics used in aquaculture can vary from year-to-year. For example, in 1992 the Norwegian salmon culture industry used 27 tonnes of antibiotics. The following year, such use dropped by 78% to 6 tonnes (Figure 1). In recent years there has been a substantial reduction in the amount of antibiotic needed per unit production owing to greater reliance on vaccination and more potent antibiotics that require less drug per treatment (Weston, 1996). It is also apparent from these data that the drug of choice in the industry can quickly shift (e.g., reduction in oxytetracycline and furazolidone use; increase in oxolinic acid and flumequine use). These industry-wide shifts can be quite rapid, complicating efforts to identify relevant research and regulatory priorities.

Unfortunately data such as those shown for Norway (Figure 1) are lacking for all other countries and industry segments. If such quantitative data were available, they would allow:

- easier recognition of cost-effectiveness so that the industry could change production practices or shift to more cost-effective alternatives;
- demonstration of market size to encourage pharmaceutical companies to develop and register (where applicable) therapeutic drugs;
- identification of particular producers who may be using chemicals in amounts far in excess of (or amounts less than) industry norms;
- protection of consumers against exposures to banned chemicals; and
- improved human health and ecological risk assessments for specific compounds.

There are several possible mechanisms to acquire these data, each having advantages and disadvantages.

Chemical producers

Pharmaceutical companies, pesticide producers and related industries currently have sales data for their products that would at least partially satisfy the identified information needs. Acquiring the data for public use, however, may be difficult because most producers would prefer such data to remain proprietary for competitive reasons, or because their products may be used in aquaculture but not registered for this purpose. In certain cases, the chemical producers themselves may be unaware of the relative proportions of their products used in aquaculture and agriculture. Wholesalers also commonly transport aquaculture chemicals across national boundaries, so that the producer may be unaware of the point of ultimate use.

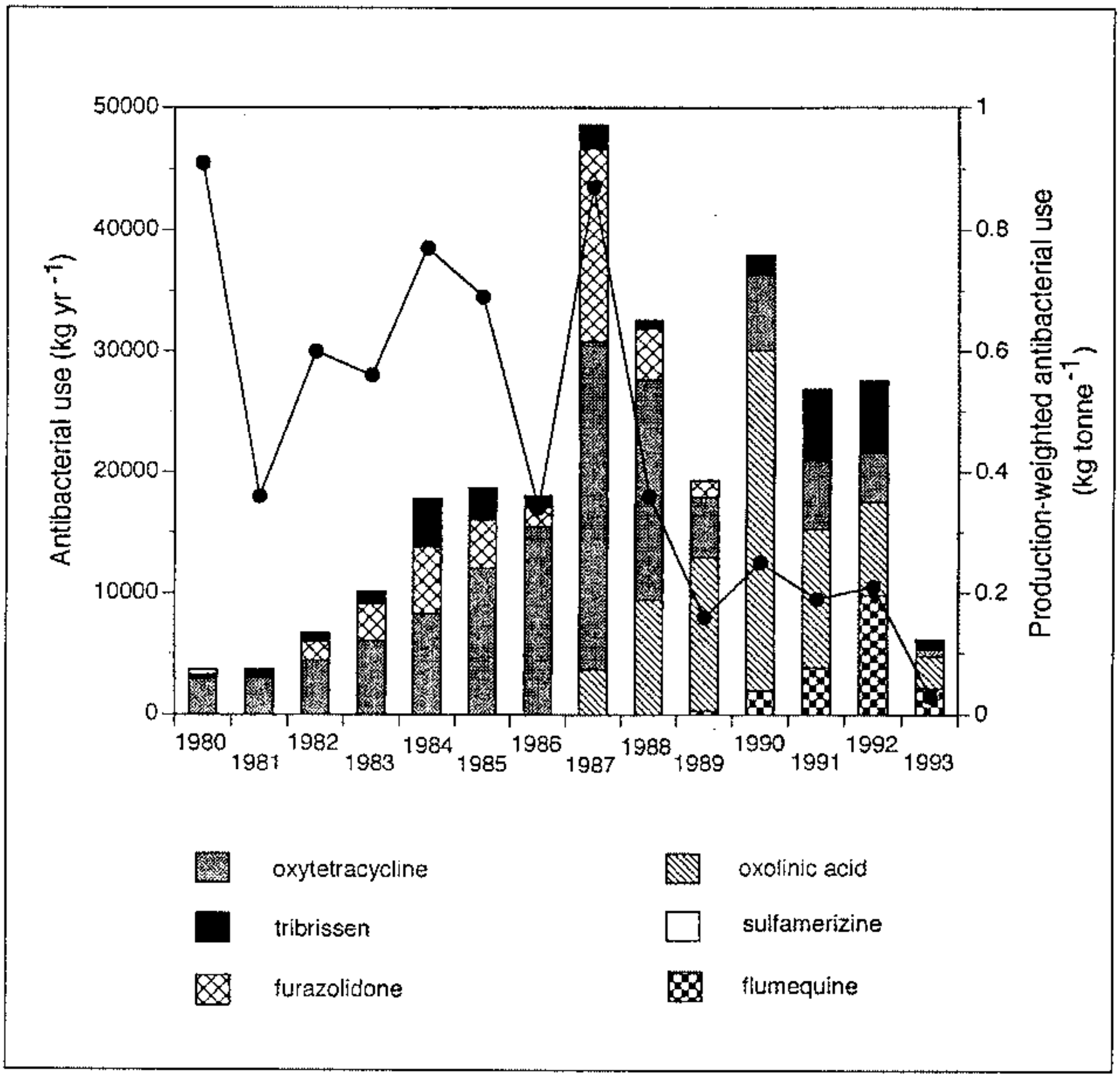

Figure 1 The amounts of antibacterials used in Norway annually for the production of Atlantic salmon and rainbow trout. The weight of active ingredients (left scale) is represented by the stacked histograms; the amount of antibacterial per unit production (right scale) is represented by the line. The scale does not show use of small quantities (<150 kg) of tribrissen in 1989, furazolidone in 1990, 1991, and 1993, and florphenicol in 1993. From Weston (1996) with data from the Norwegian Medicinal Depot and Norwegian Fish Farmers Association.

Import licensing

Importers of aquacultural chemicals could be required to obtain a license for import, as is currently the case in Thailand for aquaculture pesticides and disinfectants (Tonguthai, in press). Such a mechanism would not encompass domestically produced chemicals but in most developing countries domestic production is negligible. Illegal import without proper licensing may be a significant problem in some areas, reducing the value of quantitative data gathered by licensing procedures.

Central distribution

Quantitative data exist for Norway because all aquacultural antibacterials have been distributed through a single federally-sanctioned clearinghouse. While this system has provided country-wide data on antibacterial use, it has been criticised on the grounds of governmental interference in commerce.

Veterinary prescription

Use of chemotherapeutants in Danish trout culture requires drug dispensation by licensed veterinarians. All prescriptions are sent to federal authorities, thereby providing data on both a nation-wide basis and for individual farms. Very reliable data are provided in this manner, but the approach may be impractical in countries where veterinary support for the aquaculture industry is inadequate.

Self-reporting by aquaculturists

Such a voluntary reporting system may function in farmer groups or trade associations but may be problematic where producers are more geographically isolated or when they are not aware of the advantages of self-reporting. In most countries, it may be unrealistic to expect data to be acquired at the level of individual farms. Import licensing may be the most easily adapted mechanism that will provide reliable data at least at the national level. Authorities may also conduct detailed chemical use surveys of representative farms and obtain industry-wide estimates through extrapolation. Similarly, case studies may be undertaken on the production of chemicals and their distribution to representative aquacultural users.

4.6. Difficulties in effluent treatment

When chemicals are employed by aquaculturists, either for preventative or treatment purposes, a certain portion of the applied substance leaves the farm via the effluent or, in the case of net-cage culture, is released directly to the environment. For example, the vast majority of oxytetracycline and oxolinic acid provided is likely to leave the farm as particulate wastes because of feed wastage and poor digestive absorption of these drugs (Cravedi *et al.*, 1987). Discharge of these contaminated feeds and faeces is likely to occur continuously at low concentrations but may be greater at certain periods of the production cycle such as during tank or pond cleaning. Accumulation of solid wastes and associated chemical residues near the point of discharge is likely. For dissolved chemicals, the spatial extent of impact will depend upon dilution of the waste stream within the farm system and the rate of dilution after discharge.

In Europe and North America, environmental legislation has placed restrictions on the composition of aquaculture effluents. These regulations were primarily enacted to reduce the risks of eutrophication associated with dietary phosphorus emissions and have been very successful. Simple methods of particle removal, such as screening or use of settlement ponds, are practised globally. However, treatment of the effluent to remove dissolved constituents (e.g., nitrogenous compounds such as urea) is not commonly practised because related techniques are either expensive, still under development, or do not exist.

While methods for controlling suspended solids, BOD and nutrient discharges from aquaculture have been well studied, there are few established methods to remove residues of chemotherapeutants, pesticides and other chemicals. This is partly because few regulatory bodies have placed limits on the concentrations of such chemicals in effluent. In recent years, however, the level of regulatory scrutiny has increased. One of the few papers to examine effluent control of chemotherapeutant residues is Smith *et al.* (1994b). In studies of a salmonid hatchery, it was found that a circulating drum filter with a nominal pore size of 50 μm was very effective at removing oxytetracycline from the effluent. Oxytetracycline concentrations in the filter retentate were increased at least 500-fold over those of the original effluent and approximate mass balance calculations indicated that the filter had retained virtually all the oxytetracycline used on the farm. The retained particles were further concentrated with a sedimentation trap, in which the efficiency of oxytetracycline removal varied from 12-92%, probably as a function of the size of the particles (i.e., waste feed was retained better than faeces).

Recirculating systems provide another means of effluent control. In developed countries, recirculation technologies have provided a capital intensive method by which water quality may be accurately monitored and controlled. In aquaculture, the proportions of water reuse, levels of monitoring and methods employed in water quality maintenance vary considerably. The simplest recirculation system consists of two ponds, one of which is employed to hold animal inventory and the other as a reservoir. Water is pumped continuously from the reservoir to the stock pond in a single loop. Although offering many advantages, recirculation technologies require high capital investment and, dependent on the configuration employed, sensitive monitoring and alarm systems. Clearly, in most existing commercial settings, the opportunities for water reuse will be limited. Nevertheless, the concepts employed in totally enclosed systems and the lessons learned from use of individual components of these systems may benefit coastal pond operations. One problem that may arise is that recirculating systems can retain residual treatment chemicals, affecting the total exposure time of the cultured organisms and, potentially, the efficacy of the water purification system.

In pond-based aquaculture, various strategies may be employed to eliminate, or substantially reduce, the levels of chemicals entering receiving waters. Settlement ponds are especially useful in this regard. Some operators employ unproductive ponds for sedimentation prior to final water discharge. This tactic increases the residence time of effluent waters and permits settlement of organic materials and, where present, associated chemicals. Increased farm residence time for water also increases the likelihood of degradation and dilution of soluble chemicals before effluent discharge. A number of strategies, with low capital investment requirements, might further enhance the utility of settlement ponds. For example, sediment ploughing following pond drainage would increase aerobic degradation of sediment-associated antibacterials. The introduction of filter feeders, macrophytes, and/or other aquatic organisms into effluent ponds could provide a means to bioconcentrate and/or metabolise residual chemotherapeutants. Subsequent harvesting and incineration of these natural 'treatment' agents might substantially reduce the amount of chemicals entering receiving waters.

4.7. International trade

In the current global market, it is not unusual for a country to prohibit the use of a specific chemotherapeutant or pesticide by its own food producers because of a perceived need to protect the consumer but to import products grown elsewhere using the same chemical. For example:

- Chloramphenicol has not been approved for use in the USA and Japan, and is explicitly banned in Canada and in European Union countries. However, it is used in shrimp culture in Latin America and Asia where shrimp are grown primarily for export to European, Japanese and U.S. markets. JECFA (1995) was unable to allocate an MRL for chloramphenicol primarily for lack of information necessary to establish an ADI.

- Use of malachite green is not permitted in the USA or European Union because of concerns about its carcinogenetic properties. Nevertheless, it is used in shrimp farms that are providing products for export. This issue is of heightened concern because of new evidence indicating that the time required for elimination of malachite green residues in salmonids may be extremely long (i.e., many months; Alderman and Clifton-Hadley, 1993).

- The USA does not permit its own producers to use nitrofurans because of carcinogenicity concerns. However, salmon is imported from Scandinavia where there has been use of this drug in the past and shrimp is imported from Asian countries where these drugs are still occasionally used.

- Approval for the aquacultural use of fluoroquinolones, a new class of antibacterials, is currently delayed in the USA largely due to a desire within the medical community to protect the efficacy of these drugs by reserving their use for human therapy. Drugs of this class are, however, already in use in agriculture in Europe and are used in very limited situations (because of their cost) in aquaculture in Indonesia.

International trade of aquatic food products is governed by international agreements including the General Agreement on Tariffs and Trade and the Agreement on the Application of Sanitary and Phytosanitary Measures (GATT, 1994; FAO, 1995b). The so-called SPS Agreement stipulates that Members:

- have the right to take sanitary and phytosanitary measures necessary for the protection of human, animal or plant life or health;

- shall ensure that any sanitary or phytosanitary measure is applied only to the extent necessary to protect human, animal or plant life or health, is based on scientific principles and is not maintained without sufficient scientific evidence;

- are to base their sanitary and phytosanitary measures on international standards. Measures that comply with international standards deemed necessary to protect human, animal or plant life or health are presumed to be consistent with obligations under the agreement.

The agreement establishes the standards, guidelines, and recommendations of the FAO/WHO *Codex Alimentarius* Commission as the international reference point in trade disputes over measures to protect food safety. Upon request by the *Codex Alimentarius* Commission, the Joint WHO/FAO Expert Committee on Food Additives (JECFA) undertakes evaluations of toxicological data on food additives, contaminants and residues of veterinary drugs with a view to establishing MRLs. JECFA also estimates acceptable daily intakes (ADIs) for these substances by humans.

However, it is not in the interests of producing countries that adjudication by such international bodies becomes necessary. If it becomes necessary: 1) import of the product may be prohibited until the case is resolved; 2) opportunities for the producers' input into the resolution process, which is intended to be entirely on scientific grounds, may be very limited; and 3) the producers and traders are likely to loose substantial market share because of public attention, regardless of the resolution of the dispute.

In order to avoid the adverse public perceptions of the aquaculture industry that such confrontations may create, it would be wise for farmers in exporting countries to recognise sensitivities in their target market when selecting antibacterials. Use of chloramphenicol and malachite green, in particular, are likely to become increasingly restricted. Pursuit of alternative therapeutants should be given the highest priority.

4.8. Need for environmental fate and effects information

Alderman *et al.* (1994) attempted to provide details of all chemicals used in coastal aquaculture in the North Atlantic region with particular emphasis on their potential for producing environmental effects. Throughout this document, phrases such as "little is known" or "nothing is known" are entered for many chemicals. Most of the chemicals in the report are used in coastal aquaculture world-wide but there is still little or no scientific information available on the potential environmental effects associated with many of them. Some relevant new work is beginning to be published but mainly on the already comparatively well known antibacterials such as oxytetracycline (e.g., Smith, 1996).

Schemes governing the environmental testing, evaluation of intrinsic hazard and site specific risk analysis are in place in some countries. EU directive 81/851.EEC, which covers pharmaceutical products in general, has been further developed in the UK for aquacultural purposes into a three-tier system depending on environmental properties (Table I). Other European states, such as The

Netherlands, are developing comparable systems, while Norway already has a comprehensive regulatory system in place.

Table I

The UK tiered system for ecotoxicity testing of medicines intended for use in fish farming (from VMD, 1996)

	TIER 1	TIER 2	TIER 3
PHYSICO-CHEMICAL PROPERTIES	- Molecular weight - UV/visible absorption spectrum - Melting point - Boiling point - Vapour pressure - Water solubility - Water dissociation constant - Octanol-water partition coefficient (K_{ow})	- Sediment/water adsorption coefficient (if K_{ow} is low)	- No further requirements
FATE	- Hydrolysis half-life at pH 5, 7 and 9 - Photolysis half-life	- Biodegradation mechanism and half-life in natural sediment-water test systems (if hydrolysis and photolysis slow) - Bioconcentration tests (if K_{ow} is high and exposure likely to be long)	- Dispersion data - Outputs from computer models - Fate in sediments based microcosms or mesocosms
BIOLOGICAL EFFECTS	- Acute toxicity to one species of juvenile or larval fish - Acute toxicity to one appropriate species and stage of larval crustacean - Toxicity to one species of micro alga	- Chronic fish and crustacean reproduction, early-life-stage or growth tests (if prolonged exposure likely) - Acute toxicity to a macrophyte (if toxic to algae) - Acute toxicity to juvenile or larval molluscs (if of economic importance in area of use) - Acute and/or chronic toxicity to obligate sediment feeders (crustacea, molluscs or annelids)	- Mesocosm studies of effects on benthic fauna - Bioassays using sensitive taxa - Field investigations - Effects on microbial communities

Many chemicals can be adequately characterised by Tier 1 and the physico-chemical properties can usually be obtained at reasonable cost. As a minimum requirement, the exposures corresponding to acute biological effects should be established for a majority of compounds in the categories cited in section 2 of this report. However, where compounds with higher log K_{ow} or K_d values are concerned, the property of greatest importance for predicting long-term behaviour is probably biodegradation in sediment and/or water.

GESAMP hazard profiles for harmful substances carried by ships exist for many aquacultural chemicals other than chemotherapeutants (see Annex 1). These hazard profiles contain data on aquatic toxicity and bioaccumulation. Other sources of information are the Food and Agriculture Organization of the United Nations (FAO), the World Health Organisation (WHO), and the International Programme on Chemical Safety (e.g. JECFA, 1994). Internationally available environmental data bases may be a further source of information (e.g., AQUIRE, a toxicity data base of the U.S. Environmental Protection Agency; ECDIN, the Environmental Chemicals Data and Information Network at the DC Host Centre, Valby/Copenhagen, Denmark; IUCLID, of the CEC Chemicals Bureau, Ispra (VA), Italy).

The responsibility for hazard testing usually lies with the product manufacturer. It should be recognised that the majority of pharmaceutical products were developed for purposes other than aquaculture and that relevant data may be difficult to obtain. For more recently developed chemical products, much of this information is undoubtedly already available but often resides in confidential files owned by the manufacturer or patent holder for the product. It is considered important that such information be made more generally available.

It is very possible that if the necessary data are developed or made available, it will be recognised that the vast majority of chemicals used in coastal aquaculture, when used properly, do not present any significant threat to the environment.

4.9. Need for alternatives

The most obvious way to minimise the adverse effects of aquaculture chemicals is simply to use less of them. Several emerging technologies offer the prospect of substantial reductions in chemical use. For example, the use of liquid oxygen to maintain mild hyperoxygenation (as an alternative to a simple paddle aerator) reduces the need for chemotherapy in eel, seabass and sea bream (M. Saroglia, pers. comm.). Other alternatives to chemical use are listed below:

Recirculation systems

Recirculation systems have been developed in Thailand primarily to exclude viral pathogens (e.g., yellowhead virus and white spot virus) from the culture system. They also have the effect of reducing effluents released to the external environment. A typical scheme involves the use of sedimentation and reservoir ponds, chemical and biological treatment, and aeration. More sophisticated systems can include biofiltration, ultraviolet, ozonisation, filtration, flocculation and sludge concentration and collection units (Najamuddin *et al.*, 1996). A range of other potential water treatment modules, derived mainly from sewage treatment plants, are presently being evaluated for their use in aquaculture. The advantages of water reuse/recirculation systems with respect to chemical use are many-fold. First, the amount of effluent entering nearby water bodies is greatly reduced. Second, sealed systems safeguard the aquaculturist against entry of noxious agents (e.g., pathogens, pesticides, herbicides). Third, dependent upon configuration, recirculation systems may be employed to enhance bacterial killing (e.g., with the use of ozonisation), increase the level of antibiotic photodegradation (e.g., with ultraviolet light) and assist in the removal of suspended organic materials that may harbour pathogens and or chemical residues (sludge concentration and collection, filtration).

Bioremediation

This technology involves the addition of bacteria and enzymes to shrimp ponds to mineralise organic matter. Most bioremedial formulations originate from temperate countries and were developed for wastewater treatment. Experiments conducted in Thailand showed that the most common bioremediation agents had no advantageous effect on water quality and shrimp growth (Keachum, 1994; Lin, 1995). Despite their prohibitive costs and unproven efficacy, these products are frequently used. This highlights the predicament of shrimp farmers attempting to manage pond environments and the need for related research and information transfer.

Probiosis

Probiosis is based on the principle of competitive exclusion and involves the use of living bacteria or yeast in the diet or culture water to ensure that the gut of the cultured species is initially colonised with beneficial micro-organisms to improve digestion. This approach is being actively investigated but work is still at an early stage. There are reports from laboratories and field studies of successful competition between virulent *Vibrio* strains and non-virulent strains (e.g., Lightner *et al.*, 1992). Colonisation with desirable bacterial strains may overcome the vulnerability to pathogens observed following hatchery rearing (in which the microflora are highly modified due to long-term use of antibacterials) or use of the bacteriologically "clean" recirculating systems referred to earlier.

Immunostimulants

A number of studies (Boonyaratpalin, in press) have shown better growth, survival and disease resistance (through enhanced activity of the phagocytic cells) in salmonids, channel catfish and shrimp *Penaeus japonicus* and *P. monodon* after administration of a range of immunoenhancers including glucans and peptidoglycan. Further studies are needed to elucidate optimum treatment regimes, to characterise the immune system of shrimp and to establish the most practical and efficient methods of administration.

Vaccination

Considerable interest has emerged in the development of vaccines as tools for disease prevention to supplement the use of chemicals and thereby to promote health in aquaculture species. Unlike some chemotherapeutants, they leave no residues in the flesh of administered fish unless oil-based adjuvants are used. Although vaccination is used routinely in salmon aquaculture, effective vaccines have not yet been developed for many of the diseases important in tropical aquaculture. Moreover, the shrimp immune system is poorly understood.

Domestication

Reliance on domesticated broodstock, rather than wild organisms, could potentially help reduce the need for chemotherapeutants. Selective breeding for disease resistance is common in agriculture and should be applicable to aquaculture as well. Domestication could also contribute to the use of specific-pathogen-free (SPF) and specific-pathogen-resistant (SPR) stocks. Success of such SPF and SPR technologies, however, is highly dependent on management and the rearing environment. Thus, their development should not be construed as a panacea for all production problems.

Alternative therapeutants

Chinese aquaculture farmers are employing medicinal herbs to treat diseases such as bacterial gill rot and septicaemia (Yulin, in press). A range of herbs are used but the active ingredients are not understood.

5. CONCLUSIONS AND RECOMMENDATIONS ON THE SAFE AND EFFECTIVE USE OF CHEMICALS IN COASTAL AQUACULTURE

Use of many of the chemical classes discussed in this document is common practice in animal husbandry (e.g., use of carotenoid feed additives in the poultry industry; antibiotic use in virtually all domestic animal production). Because adoption of many of these chemicals by the aquaculture industry is a relatively new phenomenon and because of the release of residues to the aquatic environment, this practice has come under scrutiny. It is not the intent of this document to hold the aquaculture industry to higher standards than other forms of animal husbandry but, for certain chemicals and in some situations, there is legitimate cause for concern.

First, some aquacultural chemicals appear to be relatively hazardous and, on this basis alone, their use should be curtailed. Chloramphenicol is among these, as suggested by the ban imposed by a number of countries. Organotin molluscicides are also in this category, given their extremely high toxicity and their prohibition in some countries where they were previously in use. Malachite green, with its associated human health concerns, its exceptionally long persistence in aquaculture products and restrictions in the U.S. and Europe, is another example. Some have argued that dichlorvos should fall into this category (Ross, 1989) and there is reason to suggest that aquatic use of all organophosphate pesticides merits evaluation based on more detailed information on current treatment regimes.

Second, most aquacultural chemicals can be used safely if standard precautions are followed, but they can pose a threat to the environment and/or human health if misused. Excessive dosage, failure to provide for adequate neutralisation or dilution prior to discharge and lack of adequate personal protection equipment are among the factors that could make an otherwise acceptable chemical use, unsafe. In these cases, denying regulatory approval of the chemical can be unnecessarily restrictive for the aquaculture industry but education, clearer labelling and enforcement of effluent quality limits are all among the possible approaches to ensure safe use.

Finally, some aquacultural chemicals may be environmentally benign under most situations but detrimental at specific sites because of unique attributes of those sites. Proper farm siting can substantially reduce many of the environmental impacts of aquaculture (GESAMP, 1991; 1996) including the impacts of chemicals. Sites where hydrography promotes dilution reduces exposure to dissolved toxicants. Dispersion of particulate material lessens the accumulation of solid wastes near the point of discharge although care is needed to select dispersive sites that do not simply transfer the waste to accumulating sites in adjacent areas.

Assessing the risks posed by aquacultural chemicals is severely constrained by the absence of data on the environmental fate and effects of many of these compounds. Antibacterials and other therapeutants have historically been considered drugs by regulatory officials. Environmental issues associated with residues in wastewater have been largely ignored. Information is available for some pesticides (e.g., organophosphates) because, in terrestrial applications, the aquatic fate and effects of these compounds have long been a concern. However, in many instances aquacultural chemicals were not developed specifically for aquacultural use. Thus, the data needed to assess risks in the aquatic environment, and particularly marine waters, are not available.

In particular, there is little field data on the biological responses to chemical residues in receiving waters and on the concentrations of aquacultural chemicals in effluents and sediments (with the exception of oxytetracycline in sediments beneath net cages: Weston, 1996; Smith, 1996). There is also little known with regard to the interactive effects of multiple aquacultural chemicals in relation to biological effects. Predicting synergistic, additive or antagonistic effects is difficult or impossible for most chemicals, including those used in aquaculture.

From the information presented here, recommendations have been derived with the intent of promoting the safe and effective use of chemicals in coastal aquaculture. Our underlying presumption is that the use of harmful chemicals should be minimised whenever possible. Recognising that this is not always feasible given modern production requirements, the following recommendations are provided. Because governmental bodies are the primary intended audience for this document recommendations addressed to the latter are provided first, although the aquacultural industry, the chemical and pharmaceutical industries and the scientific community all have important roles.

Recommendations for governmental authorities

1. In some developing and developed countries, regulation of aquacultural chemicals is non-existent or unenforced. A system of registration for "approved" chemicals for use in aquaculture is essential in order to protect public health, the natural environment and the export economy.

2. On the basis of scientific data relevant to local environmental conditions and the species being cultured, governmental authorities should establish withdrawal periods specific to each chemotherapeutant. Governments should enforce the use of such practices, in part by adoption of a residue testing programme, and solicit aquaculture industry collaboration to ensure their effective implementation.

3. Quantitative data on the usage of aquacultural chemicals, particularly those of greatest environmental and human health concern, should be gathered as a means to determine regulatory and research priorities.

4. Opportunities should be provided for training in the safe and effective use of chemicals in aquaculture for farm workers, other aquaculture support staff and chemical sales personnel. This training could be provided by government agencies, universities or trade associations. Drug and chemical companies should support such educational efforts.

5. There is a need for enhanced collaboration among manufacturers, suppliers and users of chemicals in aquaculture. Government authorities should encourage and facilitate such collaboration and provide expert advice, where required, to promote the safe and effective use of chemicals by aquaculturists. For these purposes, it will be useful to compile and disseminate contact details of manufacturers, importers and suppliers of chemicals as well as of hatchery and farm operators and any relevant trade associations.

Recommendations for the aquaculture industry

1. Chemotherapeutants should not be the first option when combating disease but used only as a last resort after environmental conditions, nutrition and hygiene have been optimised.

2. Prophylactic treatment should be avoided since the selective pressure for development of antibacterial resistance poses a threat to the long-term efficacy of a drug.

3. When multiple chemical alternatives are available, aquaculturists should select drugs not only on the basis of efficacy data but also on available information regarding environmental persistence, potential effects on non-target organisms, propensity to stimulate microbial resistance and rate of residue elimination.

4. Aquaculturists should utilise antibacterials having as narrow a spectrum of activity as possible but without loss of efficacy, so as to minimise selective pressure for resistance in other micro-organisms.

5. In order to document cost-effectiveness and guide future treatment, aquaculturists should maintain records of chemical use including agents used, amounts, reasons for use, methods of application, dates of use, amount/number and size of stock treated, success/failure of treatments and times of harvest of treated stock.

6. Aquaculturists should not discharge to natural water bodies any effluent containing chemical residues at concentrations likely to cause adverse biological effects and should first reduce concentrations, preferably by residue removal or increased residence time, and/or by dilution with other effluent waste streams within the farm.

7. Farms in close physical proximity should collaborate in minimising the risk of contaminating of their water supplies and those of neighbouring facilities with chemical residues and drug resistant bacteria.

Recommendations for the drug and chemical industry

1. Producers of chemicals used in aquaculture should support the development of efficacy, fate and environmental effects data specific to the species and the geographical region(s) of chemical use.

2. Aquaculture chemicals should be provided to the aquaculturist with labelling and/or data sheets in the principal local language(s). Information should be provided on active ingredients, intended use, route of treatment, environmental and health hazards, species and life stage to be treated, storage conditions, expiration dates and disposal requirements. Aquaculturists should be encouraged to purchase only chemicals with complete labelling and to follow all instructions regarding their use.

Recommendations for the scientific community

1. Scientists should continue to document and quantify the frequency, severity and spatial extent of environmental alterations related to chemical use in aquacultural activities. Such efforts have been very limited to date and quantitative assessments are urgently needed by regulators and the aquaculture industry.

2. Research is needed to develop safe alternatives to chloramphenicol, malachite green and organotin molluscicides.

3. Research and development of alternatives to chemotherapy are needed including development of probiotics, bioremediation, immunostimulants and vaccines.

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Annex 1

Substances mentioned in this report for which hazard profiles exist in the GESAMP 9.1 data base on harmful substances carried by ships, kept by the International Maritime Organization (IMO).

The ratings in each of the hazard profile columns are explained on following pages.

Substances	A	B	C	D	E	Remarks
Alum (solid or in solution up to 80%) (aluminium sulphate)	0	1	0	I	0	
Ammonia (anhydrous and aqueous, 28% or less)	0	2	1	I	X	
Ammonium (dihydrogen) phosphate	0	1	0	0	0	
Ammonium sulphate	0	1	1	0	0	
Azinphos-ethyl (ISO)	+	5	3	I	XX	ChE inhibitor
Calcium hypochlorite solutions containing 1.5% and less $Ca(OCl)_2$	0	1	1	I	X	
Calcium hypochlorite solutions containing less than 15% but more than 1.5% $Ca(OCl)_2$	0	2	1	II	XX	
Calcium hypochlorite solutions containing 15% $Ca(OCl)_2$ or more	0	3	1	II	XX	
Calcium nitrate	0	0	1	I	X	
Carbaryl (sevin)	0	5	2	II	XXX	Teratogen; ChE inhibitor
Copper sulphate, anhydrous, hydrates and solutions	+	4	3	I	XX	
Diammonium (hydrogen) phosphate	0	1	0	0	0	
Dichlorvos (ISO) (Nuvan, Aquaguard)	0	5	3	II	XXX	ChE inhibitor; Carcinogen if containing epichlorohydrin as stabilizer
Ethylene diamine tetra acetic acid, di and tetra sodium salt	0	0	1	II	0	
Formaldehyde (37%-50% solution)	0	2	2	II	XX	Skin sensitizer; Carcinogen; tested for tainting
Gypsum	0	0/D	0	0	0	
Malathion (ISO)	0	5	2	I	XX	ChE inhibitor
Organotin pesticides (viz. Azocyclotin (ISO) and SSI-121)	+	5	3	II	XXX	Neurotoxic; Immunotoxic
Organotin compounds (not otherwise specified)	+	5	3	II	XXX	Neurotoxic; Immunotoxic
Potassium permanganate	0	3	1	0	X	
Rotenone (ISO)	Z	4	2	I	XX	
Sodium hypochlorite solutions containing 2% or less NaOCl	0	1	2	I	X	Skin sensitizer
Sodium hypochlorite solutions containing 20% and less but more than 2% NaOCl	0	2	2	II	XX	Skin sensitizer
Sodium hypochlorite solutions containing more than 20% NaOCl	0	3	2	II	XX	Skin sensitizer
Trichlorfon (ISO)	0	4	2	I	XX	ChE inhibitor
Urea	0	0/BOD	0	0	0	

ABBREVIATED LEGEND TO THE HAZARD PROFILES

Column A - Bioaccumulation and Tainting

+	Bioaccumulated to significant extent and known to produce a hazard to aquatic life or human health
Z	Bioaccumulated with attendant risk to aquatic organisms or human health, however with short retention of the order of one week or less
T	Liable to produce tainting of seafood
0	No evidence to support one of the above ratings (+, Z, T)

Column B - Damage to living resources

Ratings		96 hr LC50
5	Very highly toxic	< 0.1 mg/l
4	Highly toxic	0.1-1 mg/l
3	Moderately toxic	1-10 mg/l
2	Slightly toxic	10-100 mg/l
1	Practically non-toxic	100-1000 mg/l
0	Non-hazardous	> 1000 mg/l
D	Substance likely to blanket the sea-bed	
BOD	Substance with oxygen demand	

Column C - Hazard to human health by oral intake

Ratings		LD50 (laboratory mammal)
4	Highly hazardous	< 5 mg/kg
3	Moderately hazardous	5-50 mg/kg
2	Slightly hazardous	50-500 mg/kg
1	Practically non-hazardous	500-5000 mg/kg
0	Non-hazardous	> 5000 mg/kg

Column D - Hazard to human health by skin and eye contact or inhalation

II	Hazardous (severe irritation, strong sensitizer, lung injury, percutaneous toxicity, carcinogenic, or other specific long-term adverse health effect)
I	Slightly hazardous (mild irritation, weak sensitizer)
0	Non-hazardous (non-irritant, not a sensitizer)

Column E - Reduction of amenities

XXX Highly objectionable because of persistency, smell or poisonous or irritant characteristics; as a result contaminated beaches liable to be closed; also used when there is clear evidence that the substance is a human carcinogen or that the substance has the potential to produce other serious specific long-term adverse health effects in humans.

XX Moderately objectionable because of the above characteristics, but short-term effects leading only to temporary interference with use of beaches; also used when there is credible scientific evidence that the substance is an animal carcinogen but where there is no clear evidence to indicate that the material has caused cancer in humans, or when there is evidence from laboratory studies that the substance could have the potential to produce other serious specific long-term adverse health effects.

X Slightly objectionable, non-interference with use of beaches

0 No problem

Note: The descriptive terms such as highly toxic, non-hazardous, etc., were used by the original panel for the purposes of the 1973 International Conference on Marine Pollution. They have no particular significance in terms of hazard posed outside the particular circumstances addressed by that Conference and IMO Sub-Committees, i.e. marine pollution as a consequence of discharges or spillages from ships.

Reports and Studies GESAMP

The following reports and studies have been published so far. They are available from any of the organizations sponsoring GESAMP.

1. Report of the seventh session, London, 24-30 April 1975. (1975). Rep. Stud.GESAMP, (1):pag.var. Available also in French, Spanish and Russian

2. Review of harmful substances. (1976). Rep.Stud.GESAMP, (2):80 p.

3. Scientific criteria for the selection of sites for dumping of wastes into the sea. (1975). Rep.Stud. GESAMP, (3):21 p. Available also in French, Spanish and Russian

4. Report of the eighth session, Rome, 21-27 April 1976. (1976). Rep. Stud.GESAMP, (4):pag.var. Available also in French and Russian

5. Principles for developing coastal water quality criteria. (1976). Rep.Stud.GESAMP, (5):23 p.

6. Impact of oil on the marine environment. (1977). Rep.Stud.GESAMP, (6):250 p.

7. Scientific aspects of pollution arising from the exploration and exploitation of the sea-bed. (1977). Rep.Stud.GESAMP, (7):37 p.

8. Report of the ninth session, New York, 7-11 March 1977. (1977). Rep. Stud.GESAMP, (8):33 p. Available also in French and Russian

9. Report of the tenth session, Paris, 29 May - 2 June 1978. (1978). Rep. Stud.GESAMP, (9):pag.var. Available also in French, Spanish and Russian

10. Report of the eleventh session, Dubrovnik, 25-29 February 1980. (1980). Rep.Stud.GESAMP, (10):pag.var. Available also in French and Spanish

11. Marine Pollution implications of coastal area development. (1980). Rep. Stud.GESAMP, (11):114 p.

12. Monitoring biological variables related to marine pollution. (1980). Rep. Stud.GESAMP, (12):22 p. Available also in Russian

13. Interchange of pollutants between the atmosphere and the oceans. (1980). Rep.Stud.GESAMP, (13):55 p.

14. Report of the twelfth session, Geneva, 22-29 October 1981. (1981). Rep.Stud.GESAMP, (14):pag.var. Available also in French, Spanish and Russian

15. The review of the health of the oceans. (1982). Rep.Stud.GESAMP, (15):108 p.

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17. The evaluation of the hazards of harmful substances carried by ships. (1982). Rep.Stud.GESAMP, (17):pag.var.

18. Report of the thirteenth session, Geneva, 28 February - 4 March 1983. (1983). Rep.Stud.GESAMP, (18):50 p. Available also in French, Spanish and Russian

19. An oceanographic model for the dispersion of wastes disposed of in the deep sea. (1983). Rep.Stud. GESAMP, (19):182 p.

20. Marine pollution implications of ocean energy development. (1984). Rep. Stud.GESAMP, (20):44 p.

21. Report of the fourteenth session, Vienna, 26-30 March 1984. (1984). Rep.Stud.GESAMP, (21):42 p. Available also in French, Spanish and Russian

22. Review of potentially harmful substances. Cadmium, lead and tin. (1985). Rep.Stud.GESAMP, (22):114 p.

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24. Thermal discharges in the marine environment. (1984). Rep.Stud. GESAMP, (24):44 p.

25. Report of the fifteenth session, New York, 25-29 March 1985. (1985). Rep.Stud.GESAMP, (25):49 p. Available also in French, Spanish and Russian

26. Atmospheric transport of contaminants into the Mediterranean region. (1985). Rep.Stud.GESAMP, (26):53 p.

27. Report of the sixteenth session, London, 17-21 March 1986. (1986). Rep. Stud.GESAMP, (27):74 p. Available also in French, Spanish and Russian

28. Review of potentially harmful substances. Arsenic, mercury and selenium. (1986). Rep.Stud. GESAMP, (28):172 p.

29. Review of potentially harmful substances. Organosilicon compounds (silanes and siloxanes). (1986). Published as UNEP Reg.Seas Rep.Stud., (78):24 p.

30. Environmental capacity. An approach to marine pollution prevention. (1986). Rep.Stud.GESAMP, (30):49 p.

31. Report of the seventeenth session, Rome, 30 March - 3 April 1987. (1987). Rep.Stud.GESAMP, (31):36 p. Available also in French, Spanish and Russian

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33. Report on the eighteenth session, Paris, 11-15 April 1988. (1988). Rep. Stud.GESAMP, (33):56 p. Available also in French, Spanish and Russian

34. Review of potentially harmful substances. Nutrients. (1990). Rep.Stud. GESAMP, (34):40 p.

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38. Atmospheric input of trace species to the world ocean. (1989). Rep.Stud. GESAMP, (38):111 p.

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40. Long-term consequences of low-level marine contamination: An analytical approach. (1989). Rep. Stud.GESAMP, (40):14 p.

41. Report of the twentieth session, Geneva, 7-11 May 1990. (1990). Rep. Stud.GESAMP, (41):32 p. Available also in French, Spanish and Russian

42. Review of potentially harmful substances. Choosing priority organochlorines for marine hazard assessment. (1990). Rep.Stud. GESAMP, (42):10 p.

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47. Reducing environmental impacts of coastal aquaculture. (1991). Rep. Stud.GESAMP, (47):35 p.

48. Global changes and the air-sea exchange of chemicals. (1991). Rep. Stud.GESAMP, (48):69 p.

49. Report of the twenty-second session, Vienna, 9-13 February 1992. (1992). Rep.Stud.GESAMP, (49):56 p. Available also in French, Spanish and Russian

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55. Biological indicators and their use in the measurement of the condition of the marine eenvironment. (1995). Rep.Stud.GESAMP, (55):56 p. Available also in Russian

56. Report of the twenty-fifth session, Rome, 24-28 April 1995. (1995). Rep. Stud.GESAMP, (56):54 p. Available also in French, Spanish and Russian

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62. Marine biodiversity: patterns, threats and development of a strategy for conservation. (in press). Rep.Stud.GESAMP, (62)

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