# Chemical Usage in Aquaculture: Implications for Residues in Market Products

Paul Johnston, David Santillo
Greenpeace Research Laboratories
Technical Note 06/2002

Department of Biological Sciences
University of Exeter, UK

June 2002

GRL-TN-06-2002

Publ: Greenpeace Research Laboratories, Department of Biological Sciences, University of Exeter EX4 4PS, UK

## Introduction

The culture of finfishes and shellfishes now accounts for some 30 million tonnes of production worldwide. The widespread decline (through overfishing) of many species targeted in capture fisheries continues to drive expansion of the aquaculture industry.

Diseases occur in both natural and cultured animals and can be categorised broadly into two groups:

1) Infectious diseases where the causative agent is bacterial, viral or parasitic.
2) Non-infectious diseases caused by toxic substances, improper nutrition, poor water quality, physical damage or genetics.

Infectious diseases are a major concern in aquaculture both in terms of the potential negative impacts on production and the potential for disease impacts on wild populations. Outbreaks of disease are typically caused by widely distributed, opportunistic pathogens. In natural systems they have a low prevalence and low intensity of infection, but in finfish cultures or shellfish hatcheries where stresses lower resistance and stocking density facilitates transmission of disease, impacts of disease outbreaks can be severe.

Total prevention of disease in aquacultural systems is likely to be unattainable in practice even though pathogen free broodstock for *e.g.* shrimp aquaculture is available. Disease management, therefore, depends upon good culture practice in combination with chemotherapeutic agents. Some agents may be administered (often in feed) on a prophylactic basis, although in many countries, the US for example, this is forbidden. Parasiticides, anaesthetics, spawning hormones, oxidants, disinfectants and herbicides are all routinely used. In the case of antibiotics, the development of vaccines has led to a sharp reduction in use in many of the finfish cultures in Europe and North America.

Even though chemical usage is widespread in the aquaculture industry, and the generic chemicals in use are known, accurate statistics on useage are hard to come by. As pointed out in a recent comprehensive review of chemical use in the south-east Asian sector (Gräslund & Bengtsson, 2001), despite the importance of this industry, documentation of the quality and quantity of chemicals and biological products used is scarce. The import industry is a substantial one. Nearly 27,000 tonnes of prawns and shrimps with a value of around GBP 125 million were imported into the UK alone in 1997. While the microbiological quality of these is closely monitored, chemical residues have received little attention.

The issue of chemical residues present in seafood, particularly antibiotics, has been thrown into sharp relief by reports of residues of nitrofuran antibacterials being detected in shrimps imported into the EU from Vietnam and from Thailand. Nitrofuran antibacterials are veterinary drugs whose use in food producing animals and fish is banned in the EU because of health concerns, including a possible increase in cancer risk in humans. Chloramphenicol has been detected in shrimps imported from Myanmar, Burma. Chloramphenicol, a broad spectrum antibiotic which has latterly been associated with aplastic anaemia in humans, has been banned in the EU for use in food producing animals and fish. This is a drug of last resort in human medicine for *Salmonella typhimurium* infections. The EC has responded to these findings by imposing a requirement on member states to monitor imported shrimp from these areas for the specific residues. (Commission

Decisions: 2002/249/EC; 2002/250/EC; 2002/251/EC, CEC 2002a,b,c). At the same time, there are relatively few constraints on chemical usage in aquaculture and many antibiotics are widely available.

## Results of current literature review

The identification of antibiotics in imported shrimp has led to extensive coverage of the issue in the international media and, as noted above, led to EC imposition of monitoring. In relation to coverage of this and related issues in the scientific literature, interrogation of the in-house Science Unit literature database and on-line British Library resources generated a general review (cited above) on classes and types of chemicals used in aquaculture. No quantitative data were included in this review (Gräslund & Bengtsson 2001).

Antibiotic residues have been detected in a small proportion (8-9%) of tiger prawns tested in the UK (Willis *et al.* 1999). Of 204 prawns tested in 1994, one contained detectable oxolinic acid (a quinolone antibacterial), one contained sulphonamides and 16 showed the presence of oxytetracycline. A more recent evaluation using 98 samples from 17 producers spread over 3 countries showed that of these, 23 showed antibiotic activity. 18 contained residues of the antibiotic trimethoprim and 3 of these also contained gentamicin. The agents responsible for the activity in the remaining seven samples were not identified. Chloramphenicol and oxytetracycline were not found. This issue was flagged by the authors as requiring ongoing surveillance.

Various other articles in the specialist journals have dealt with the issue of antibiotic resistance (*e.g.* Sorum 1999 & 2000) and the impact of vaccines on reducing drug use is acknowledged for the Scandinavian sector. An extensive descriptive literature exists on the various diseases which can impact diverse aquaculture operations while others focus on the treatment regimes derived for specific problems. While many these papers contain information of interest, they do not address the issue of residues of chemicals present in the marketed products

Some articles in the literature provide quantitative data on antibiotic usage in aquaculture. These have already been referred to in Johnston *et al.* (1998). Such data have primarily been derived from the Scandinavian and North American aquaculture sector. GESAMP (1997) also provide information on the broad classes of chemicals in use in aquaculture, but provide no quantitative data or information on usage patterns.

With respect to the implications of residues in marketed products, while many papers make generic reference to this as established fact and, therefore, of general concern, there are few data in the literature. Even more general searching of internet resources simply retrieved reporting of the chloramphenicol and nitrofuran issue, together with many resources documenting the identity of chemicals in use in the sector. Other resources detail products registered for use in various legislatures.

In relation to detection of bacteria/viruses in marketed product, little if any information exists, although antibiotic resistance in sediment bacteria impacted by aquaculture activities is now well documented. In addition, the focus of the little research carried out to date has been on antibiotic residues. No data were found on other chemicals such as pesticides and antifoulants known to be used in the sector. Finally, no data were found on residues of synthetic chemicals such as dioxins and PCBs transferred via feedstuffs in use in aquaculture beyond information already reported in EC Reports (see: *e.g*. EC 2000), largely from regulatory surveillance programmes.

Overall, the coverage of this issue in the technical literature suggests that, while the potential for problems is high, it remains poorly researched. A similar conclusion was reached by Gräslund and Bengtsson (2001) in relation to shrimp aquaculture:-

*"Theoretically, chemicals other than antibiotics that are added to the shrimp ponds, or by-products from the applied substances, that have a bioaccumulation potential, could be found as residues in the shrimps. …However, little attention has been paid to the risk of residues other than antibiotics in farmed shrimps, and no data from such investigations have been found".*

## Point of departure for further campaign discussion

Some detailed background on the various chemicals and groups of chemicals used in aquaculture, together with a broad outline of the environmental problems they can cause, is already provided in the 1998 Greenpeace Report on the World's Oceans (Johnston *et al*. 1998). Following on from the additional concerns raised above regarding residues carried over into seafood, this document outlines (in Table 1) those chemicals reportedly used in aquaculture (shrimp and finfish) world-wide which, by virtue of their intrinsic properties, may render them of concern with regard to consumer health.

This is not intended to provide an exhaustive review of their toxicologies, nor to attempt to establish relative levels of hazard; indeed, there is largely insufficient information on which to base such judgments. Rather, Table 1 provides a condensed overview of those chemical agents which may be of greatest concern on the basis of their toxicity and likelihood to persist and/or accumulate in biological tissues, as a starting point for identification of priorities for further research (including, as practicable and necessary, analytical determinations).

**Table 1: Summary of chemicals used in the culture of finfish and/or shrimps which are, or may be, of concern with respect to residues in the final seafood product based on their intrinsic properties and/or reported detection of residues in foodstuffs.**

| **Chemical** | **Trade names** | **Chemical type** | **Use Category** | **Hazards** | **References** | **Notes** |
|---|---|---|---|---|---|---|
| Acriflavine neutral (mixture of 3,6-diamino-10-methylacrid-inium chloride and 3,6-diamino-acridine) CAS: 8048-52-0 | Euflavine, Gonacrine, Neutroflavine, Trypaflavine | | Antibacterial and external topical treatment for protozoan infection – used on fish eggs and fry | Irritant Inhibitor of DNA activity in human cell lines (has been used as anti-inflamm-atory drug) | GESAMP (1997) Choi *et al.* (2000) [MSDS available at http://www.koivet.com/acriflavine_msds.html] | Acroflavine hydrochloride (CAS 8063-24-9) is a suspected teratogen, but appears to be used less frequently |
| Amoxycillin (Amoxicillin) CAS: 61336-70-7 | | ß-lactam antibiotic | Antibacterial administered in feed or, more rarely, by direct injection | Exposure of consumers sensitive to ß-lactam (penicillin-type) antibiotics Development of resistant strains | GESAMP (1997) | |
| Azamethiphos CAS: 35575-96-3 | Salmosan 50% plus several others | Organophosphate | Treatment against preadult and adult sealice in European and North American salmon culture | Acetylcholine esterase inhibition | Pretti *et al.* (2002) | |
| Azinphos ethyl CAS: 2642-71-9 | Gusathion A | Organophosphate | Previously used to remove molluscs from shrimp ponds in Philippines, but now banned. Use in other countries not documented | Acetylcholine esterase inhibition | Budavari (1996), Graslund & Bengtsson (2001) | |
| Benzocaine (ethyl *para*-amino-benzoate) CAS: 94-09-7 | Anesthone, Orthesin, Cepacaine plus many others | Aminobenzoate | Anaesthetic used during egg and milt-stripping and as preparation for transport | Harmful if swallowed Residues can be detected in fish tissue, though more rapidly cleared than other anaesthetics | GESAMP (1997), Meinertz *et al.* (1999) | Developed in response to concerns about tricaine methane-sulphonate (Meinertz *et al.* 1999) |
| Carbaryl | Sevin | Organophosphate/Car | Control of burrowing | Teratogen | GESAMP (1997), | |

| | | | | | | |
|---|---|---|---|---|---|---|
| CAS: 63-25-2 | | bamate | shrimp in shrimp ponds in Central and S. America, and in bottom oyster culture in NW USA | Acetylcholine esterase inhibition | Dumbauld *et al.* (2001) | |
| n-Chloro-*p*-toluene sulfonamide, sodium salt<br>CAS: 127-65-1 | Chloramine-T | Chlorinated sulphonamide | Treatment of bacterial gill disease and protozoan ectoparasites in salmonids<br>Disinfectant used for tank and equipment cleaning | Harmful by ingestion<br>Active ingredient is 20% available chlorine – no information on redidues | [MSDS available at http://www.cris.com/~hschem/msdscht.html | |
| Chloramphenicol<br>CAS: 56-75-7 | | "Phenicol" antibiotic | Broad spectrum antibiotic | Aplastic anaemia<br>Resistant strains develop readily | Primavera *et al.* (1993), Budavari (1996), GESAMP (1997) Graslund & Bengtsson (2001) | |
| Chlorpyrifos<br>CAS: 2921-88-2 | Dursban plus many others | Organophosphate | Control of ectoparasites in freshwater fish and of monogenetic trematode infections in shrimp hatcheries | Acetylcholine esterase inhibition<br>Neurotoxicity greater in juvenile animals | GESAMP (1997), Chanda *et al.* (2002) | |
| Cotrimoxazole (Sulfamethox-azole)<br>CAS: 723-46-6 | | Sulphonamide antibiotic | General antibacterial | Toxic epidermal necrolysis in sensitive individuals | GESAMP (1997), Nassif *et al.* (2002) | |
| Cypermethrin<br>CAS: 52315-07-8 | EXCIS plus many others | Synthetic pyrethroid | Net pen treatment of sealice on salmonids in USA, UK, Norway, Faroes and Ireland | Neurotoxicity, possibly enhanced by co-presence of organophosphates | Roth (2000), Ernst *et al.* (2001), Haya *et al.* (2001) | Weakly antioestrogenic and antiadrogenic<br>May degrade to produce oestrogenic residues (Tyler *et al.*, 2000) |
| Deltamethrin<br>CAS: 52918-63-5 | Alpha Max plus many others | Synthetic pyrethroid | Net pen treatment of sealice on salmonids in Norway | Neurotoxicity | Roth (2000) | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Diazinon<br>CAS: 333-41-5 | Dimpylat | Organophosphate | Removal of mysids from shrimp ponds in Indonesia | Acetylcholine esterase inhibition | GESAMP (1997), Graslund & Bengtsson (2001) | |
| Dichlorvos<br>CAS: 62-73-7 | DDVP, Nuvan | Organophosphate | Widely used to control crustacean ectoparasites (sealice) in fish, especially salmonids in NW Europe and Chile – discontinued in Norway and Faroes in 1998 | Acetylcholine esterase inhibition | Budavari (1996), GESAMP (1997), Roth (2000), Graslund & Bengtsson (2001) | Di-n-butyl phthalate may be used as carrier (Burridge and Haya 1995). Some preparations may contain epichlorohydrin as a stabiliser (GESAMP 1997) |
| Diflubenzuron<br>CAS: 35367-38-5 | Dimilin, Difluron plus many others | Difluorobenzoyl urea insect growth regulator | Control of sealice in finfish culture in Norway and Chile | Cytotoxicity in human and rat cell lines | De Sousa *et al.* (1997), Roth (2000) | |
| Diquat bromide (1,1-ethylene-2,2'-bipyridinium dibromide)<br>CAS: 85-00-7 | Aquacide plus many others | | No specific information | Possible reproductive toxicant and effects on kidneys in humans<br>Highly toxic by skin contact | Goldburg *et al.* (2001)<br>[MSDS available at http://www.state.nj.us/health/eoh/rtkweb/0808.pdf] | |
| Dimethyl-5-nitroimidazole<br>CAS: 551-92-8 | Dimatridazole | Imidazole | Used against protozoan infections, though mainly for the aquarium trade | No information | GESAMP (1997) | |
| Doramectin<br>CAS: 117704-25-3 | | Avermectin | Broad spectrum endo- and ecto-parasiticide, listed as used in Chile | Reproductive toxin in rabbits<br>Relatively persistent as parent compound in liver | Baynes *et al.* (1999), Roth (2000) | |
| Emamectin benzoate<br>CAS: 137512-74-4 | Emamectin,<br>MK-0244 | Avermectin | Used against ectoparasites on salmonids in Norway, UK, Canada and Chile | Possible neurotoxicity in mammals, though not in birds | O'Grodnick *et al.* (1998), Roth (2000), Duston and Cusack (2002) | |
| Endosulfan (Thiosulfan) | Thiodan | Organochlorine | Used in shrimp farming in Thailand | Possible reproductive and immunotoxicant | Banerjee and Hussain (1986), ATSDR | Banned in numerous countries, and |

| | | | | | | |
|---|---|---|---|---|---|---|
| CAS: 115-29-7 | | | (precise use not listed) | in humans<br>Suspected endocrine disruptor | (1993), Vonier *et al.* (1996), Graslund and Bengtsson (2001) | variously classified as "toxic" and "hazardous". Breakdown product, endosulfan sulphate, is more persistent and exhibits similar toxic traits |
| Enrofloxacin<br>CAS: 93106-60-6 | | Fluoroquinolone antibiotic | Broad spectrum antibacterial | Causes retinal degeneration in cats<br>Potentially highly persistent | GESAMP (1997), Graslund and Bengtsson (2001) | |
| Erythromycin<br>CAS: 114-07-8 | | Macrolide antibiotic | Used against bacterial kidney disease and streptacoccosis in yellowtail in Japan and in SE Asia shrimp hatcheries | Development of resistant strains | Primavera *et al.* (1993), GESAMP (1997), Graslund and Bengtsson (2001) | |
| Ethoxyquin<br>CAS: 91-53-2 | | Organonitrogen antioxidant | Commonly used in feed preservation | Harmful by ingestion<br>Irritant | GESAMP (1997) [MSDS available at http://ntp-server.niehs.nih.gov/htdocs/CHEM_H&S/NTP_Chem9/Radian91-53-2.html] | |
| Furazolidone<br>CAS: 67-45-8 | | Nitrofuran antibiotic | Broad spectrum antibacterial and antiprotozoal activity | Possible human carcinogen<br>Has been used as drug for AIDS patients | GESAMP (1997), Graslund and Bengtsson (2001) | Use for food animals prohibited within EU |
| Ivermectin<br>CAS: 70288-86-7 | Ivomec | Avermectin | Used against crustacean (sealice) and nematode infestations in salmonids, including in UK, Ireland, | Neurotoxic in mammals<br>"Safe" residue levels in low ppb range for meat products | Baynes *et al.* (1999), Grant and Briggs (1998), Roth (2000) | |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | Canada and Chile | | | |
| Malachite green oxalate<br>CAS: 569-64-2 | Malachite green<br>Basic Green 4<br>Diamond Green | Organonitrogen compound | Antifungal and antiprotozoal bath treatment, primarily in shrimp hatcheries | Respiratory poison<br>Persistent residues in tissues of seafood | Primavera *et al.* (1993), Dierberg and Kiattisimkul (1996), GESAMP (1997), Graslund and Bengtsson (2001) | Prohibited for use in USA, EU and in Thailand |
| Methylene blue<br>CAS: 61-73-4 | | | Used as antifungal and antiprotozoal treatment, though less frequently than malachite green | Can produce haemolytic anaemia in laboratory animals | GESAMP (1997), Hejtmancik *et al.* (2002) | |
| Malathion<br>CAS: 121-75-5 | | Organophosphate | Control of ectoparasitic crustaceans (sealice) and trematode infections in shrimp hatcheries | Acetylcholine esterase inhibition | Budavari (1996), GESAMP (1997), Graslund and Bengtsson (2001) | |
| Metronidazole<br>CAS: 443-48-1 | | Imidazole | Used against protozoan infections, though mainly for the aquarium trade | Reasonably anticipated to be a human carcinogen | GESAMP (1997)<br>NTP (2001) | |
| 6-[2-(5-nitrofur-anyl)ethenyl]-2-pyridinemethanol<br>CAS: 13411-16-0 | Nifurpirinol | Nitrofuran | Broad spectrum and potent antibacterial and antiprotozoal agent | Suspected human carcinogen | GESAMP (1997), Graslund and Bengtsson (2001) | In 1990, one of the most common therapeutic agents used in shrimp hatcheries in the Philippines (Baticados *et al.*1990) |
| Norfloxacin<br>CAS: 70458-96-7 | Noroxin | Organonitrogen compound | Antibiotic | Used as human drug, but only for severe infections<br>(and never for children or pregnant women) | Budavari (1996), GESAMP (1997) | |
| 5-(4,5-dimeth-oxy-2- | Ormetoprim - one | Diaminopyri-midine | Applied in feed to | No information on | GESAMP (1997), | Cooking does reduce |

| | | | | | | |
|---|---|---|---|---|---|---|
| methyl-benzyl)-2,4-diaminopyrim-idine CAS: 6981-18-6 | component of ROMET-30 | antibiotic | treat furunculosis, enteric red mouth disease and vibriosis | toxicity | | tissue residues in fish (Xu *et al.* 1996) |
| Oxolinic acid CAS: 14698-29-4 | Gramurin, Dioxacin plus others | 4-quinolone antibiotic | Used against gram-negative bacteria | Development of resistant strains Residues resistant to degradation | GESAMP (1997) | |
| Oxytetracycline CAS: 79-57-2 | Terramycin, plus many others | Tetracycline antibiotic | Probably the most widely used antibacterial agent in shrimp aquaculture, especially in SE Asia | Development of strains resistant to oxytetracycline and other related antibiotics | Baticados *et al.* (1990), Primavera *et al.* (1993), GESAMP (1997), Graslund and Bengtsson (2001) | |
| Polyvinyl pyrrolidone iodine complex CAS: 25655-41-8 | Povidone iodine | Iodophore | Antibacterial and antiviral agent, used to treat fish eggs | | Budavari (1996), GESAMP (1997) | |
| Rifampicin CAS: 13292-46-1 | Rifampin plus many others | | Antibacterial, effective against mycobacterial infections | Rapid development of resistant strains | Primavera *et al.* (1993), Graslund and Bengtsson (2001) | Rifampicin resistance very common in fish and prawn from South India (Vivekanandhan *et al.* 2002) |
| Romet 30 | See Ormetoprim and Sulfadiazine | | | | | |
| Simazine CAS: 122-34-9 | Simadex, Aquazine plus many others | Triazine herbicide | No specific information | Toxic by ingestion Effects on liver and thyroid in humans Potential reproductive toxin | Goldburg *et al.* (2001) | |
| Sulfadiazine CAS: 68-35-9 | One component of ROMET-30 | Sulphonamide antibiotic | Commonly used in combination with diamino-pyrimidine to yield broad spectrum antibacterial action | Development of resistant strains | Budavari (1996), GESAMP (1997) | Cooking does reduce tissue residues in fish (Xu *et al.* 1996) |
| Sulfadimethoxine (6-Sulfanilamido-2,4-dimethoxy- | Dinosol | Sulfonamide antibiotic | No specific information | No information available | [MSDS available at http://www.vedco.com/VedcoCatalog.htm | Residues detectable in fish tissues |

| | | | | | | |
|---|---|---|---|---|---|---|
| pyrimidine)<br>CAS: 122-11-2 | | | | | l] | |
| Teflubenzuron (N-(((3,5-dichloro-2,4-difluorophenyl)amino)carbonyl)-2,6-difluoro-benzamide)<br>CAS: 83121-18-0 | Nomolt, Dart, Diaract, Tefluron | Benzoyl phenyl-urea insect growth regulator | Control of sealice in finfish culture in Norway, Canada and Chile | No information available | Roth (2000) | Residues detectable in vegetables and fruits following agricultural use |
| Tricaine methane-sulphonate (Ethyl 3-aminobenzoate, methanesulfonic acid salt)<br>CAS: 886-86-2 | Metacaine, Finquel, MS-222 | | Anaesthetic | Persistent residues in fish tissues | Meinertz *et al.* (1999) | |
| Trichlorfon<br>CAS: 52-68-6 | Dipterex, Neguvon | Organophosphate | Used against monogenean ectoparasites in Mediterranean seabass and sea bream, though also has application in shrimp culture in SE Asia | Acetylcholine esterase inhibition<br>Hydrolyses to form more toxic and persistent dichlorvos | Budavari (1996), GESAMP (1997), Graslund and Bengtsson (2001) | |
| Trifluralin<br>CAS: 1582-09-8 | Treflan | Organonitrogen compound | Fungicide used in bath treatments in shrimp aquaculture | Possible human carcinogen<br>Induces thyroid and liver tumours in mammals | Budavari (1996), GESAMP (1997), Hurley *et al.* (1998), Gunier *et al.* (2001) | |
| Trimetoprim (trimethoprim)<br>CAS: 738-70-5 | Proloprim, Trimpex plus many others | | | Potential development of antibiotic resistance<br>Residues detected in cooked prawns imported to UK from Malaysia and Thailand | Willis *et al.* (1999), Graslund and Bengtsson (2001)<br>[MSDS available at http://ntp-server.niehs.nih.gov/htdocs/CHEM_H&S/NTP_Chem7/Radian | |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | | | 738-70-5.html] | |
| Triphenyl tin acetate CAS: 900-95-8 | Fentin acetate, Brestan | Organotin compound | Previously used as antifoulant on fish cages and to remove molluscs from shrimp ponds in SE Asia | Immunotocicity in mammals<br>Possible neurotoxicity<br>Residues accumulate in fish cultured in treated ponds and persist for many months | Budavari (1996), GESAMP (1997) | Use banned in USA and Europe, as well as in Philippines and Indonesia |
| Triphenyl tin chloride CAS: 639-58-7 | Fentin chloride, Aquatin | Organotin compound | Previously used as antifoulant on fish cages and to remove molluscs from shrimp ponds in SE Asia | Immunotocicity in mammals<br>Possible neurotoxicity | Budavari (1996), GESAMP (1997) | Use banned in USA and Europe, as well as in Philippines and Indonesia |

## References


ATSDR (1993). Toxicological Profile for Endosulfan. United States Public Health Service, Agency for Toxic Substances and Disease Registry.

Banerjee, B.D. & Hussain, Q.Z. (1986) Effect of sub-chronic endosulfan exposure on humoral and cell-mediated immune responses in albino rats. *Archives of Toxicology* 59: 279-284

Baticados, M.C.L., Lavilla-Pitoga, C.R., Cruz-Lacierda, E.R., de la Peña, L.D. & Suñaz, N.A. (1990) Studies on the chemical control of luminous bacteria *Vibrio harveyi* and *V. splendidus* isolated from diseased *Penaeus monodon* larvae and rearing water. *Diseases of Aquatic Organisms* 9: 133-139

Baynes, R.E., Martín-Jiménez, T., Craigmill, A.L. & Riviere, J.E. (1999) Estimating Provisional Acceptable Residues for Extralabel Drug Use in Livestock. *Regulatory Toxicology and Pharmacology* 29: 287–299

Budavari, S.M., O'Neil, J., Smith A. & Heckleman P.E. [Eds] (1989) The Merck index: an encyclopaedia of chemicals, drugs and biologicals. 11th Edn, Merck and Co, Inc., New Jersey, USA

CEC (2002a) Commission Decision (2002/249/EC) concerning certain protective measures with regard to certain fishery and aquaculture products intended for human consumption and imported from Myanmar http://europa.eu.int/eur-lex/en/dat/2002/l_084/l_08420020328en00730074.pdf

CEC (2002b) Commission Decision (2002/250/EC) concerning the extension of the protective measures provided by Decision 2001/699/EC, with regard to the fishery and aquaculture products imported from Vietnam http://europa.eu.int/eur-lex/en/dat/2002/l_084/l_08420020328en00750076.pdf

CEC (2002c) Commission Decision (2002/251/EC) concerning certain protective measures with regard to poultrymeat and certain fishery and aquaculture products intended for human consumption and imported from Thailand http://europa.eu.int/eurlex/en/dat/2002/l_084/l_08420020328en00770078.pdf

Chanda, S.M., Lassiter, T.L., Moser, V.C., Barone, S. & Padilla, S. (2002) Tissue carboxylesterases and chlorpyrifos toxicity in the developing rat**.** *Human and Ecological Risk Assessment* 8(1): 75-90

Choi, S.H., Cho, J.Y., Chung, Y.S., Hong, E.-K., Han, Y.-B. & Kim, S.G. (2000) Inhibition of lipopolysaccharide-induced I-êB degradation and tumor necrosis factor-á expression by acriflavine, an antimicrobial agent. *International Journal of Immunopharmacology* 22: 775-787

Dierberg, F.E & Kiattisimkul, W. (1996) Issues, impacts and implications of shrimp aquaculture in Thailand. *Environmental Management* 20: 649-666

Dumbauld, B.R., Brooks, K.M. & Posey, M.H. (2001) Response of an estuarine benthic community to application of the pesticide carbaryl and cultivation of pacific oysters (*Crassostrea gigas*) in Willapa Bay, Washington. *Marine Pollution Bulletin* 42(10): 826-844

Duston, J. & Cusack, R.R. (2002) Emamectin benzoate: an effective in-feed treatment against the gill parasite *Salmincola edwardsii* on brook trout. *Aquaculture* 207(1-2): 1-9

EC (2000) Reports on Tasks for Scientific Cooperation. Assessment of dietary intake of dioxins and related PCBs by the population of EU Member States. Publ. European Commission Health and Consumer Protection Directorate General, 7 June 2000

Ernst, W., Jackman, P., Doe, K., Page, F., Julien, G., Mackay, K. & Sutherland, T. (2001) Dispersion and toxicity to non-target aquatic organisms of pesticides used to treat sea lice on salmon in net pen enclosures. *Marine Pollution Bulletin* 42(6): 433-444

Haya, K., Burridge, L.E. & Chang, B.D. (2001) Environmental impact of chemical wastes produced by the salmon aquaculture industry. *ICES Journal of Marine Science* 58(2): 492-496

Hejtmancik, M.R., Ryan, M.J., Toft, J.D., Persing, R.L., Kurtz, P.J. & Chabra, R.S. (2002) Hematological effects in F344 rats and B6C3F1 mice during the 13-week gavage toxicity study of methylene blue trihydrate. *Toxicological Sciences* 65 (1): 126-134

GESAMP (1997) Towards safe and effective use of chemicals in coastal aquaculture. GESAMP Reports and Studies No: 65 Publ. IMO/FAO/UNESCO/IOC/WMO/WHO/IAEA/ UN/UNEP., FAO Rome.

Goldburg, R.J., Elliot, M.S. & Naylor, R.L. (2001) Marine Aquaculture in the United States: Environmental Impacts and Policy Options, Pew Oceans Commission, Arlington, Virginia: 33 pp.

Grant, A. & Briggs, A.D. (1998) Use of ivermectin in marine fish farms: some concerns. *Marine Pollution Bulletin* 36(8): 566-568

Gräslund, S. & Bengtsson, B.-E. (2001) Chemicals and biological products used in south-east Asian shrimp farming, and their potential impact on the environment – a review. *The Science of the Total Environment* 280: 93-131

Gunier, R.B., Harnly, M.E., Reynolds, P., Hertz, A. & von Behren, J. (2001) Agricultural pesticide use in California: Pesticide prioritization, use densities, and population distributions for a childhood cancer study. *Environmental Health Perspectives* 109(10): 1071-1078

Hurley, P.M., Hill, R.N. & Whiting, R.J. (1998) Mode of carcinogenic action of pesticides inducing thyroid follicular cell tumors in rodents. *Environmental Health Perspectives* 106 (8): 437-445

Johnston, P., Santillo, D., Stringer, R., Ashton, J., McKay, B., Verbeek, M., Jackson, E., Landman, J., van den Broek, J., Samsom, D., & Simmonds, M. (1998) Greenpeace Report on the World's Oceans. Greenpeace Research Laboratories Report, May 1998. Publ: Stichting Greenpeace Council. ISBN: 90/73361/45/1: 154 pp.

Meinertz, J.R., Stehly, G.R., Hubert, T.D. & Bernardy, J.A. (1999) Liquid chromatographic determination of benzocaine and N-acetylbenzocaine in the edible fillet tissue from rainbow trout. *Journal of Chromatography A* 855: 255–260

Nassif, A., Bensussan, A., Dorothee, G., Mani-Chouaib, F., Bachot, N., Bagot, M., Boumsell, L. & Roujeau, J.C. (2002) Drug specific cytotoxic T-cells in the skin lesions of a patient with toxic epidermal necrolysis. *Journal of Investigative Dermatology* 118 (4): 728-733

NTP (2001) United States Department of Health and Human Services, Public Health Service, National Toxicology Program, 9th Report on Carcinogens, Revised January 2001

O'Grodnick, J.S., Wislocki, P.G., Keenan, K.P., Beavers, J.B., Frey, L.T. & Jaber, M. (1998) Subchronic and reproductive toxicity of emamectin benzoate to mallard ducks and northern bobwhite quail. *Environmental Toxicology and Chemistry* 17(11): 2318-2324

Pretti, C., Soldani, G., Cognetti-Varriale, A.M., Monni, G., Meucci, V. & Intorre, L. (2002) Efficacy and safety of azamethiphos for the treatment of pseudodactylogyrosis in the European eel. *Journal of Veterinary Pharmacology and Therapeutics* 25(2): 155-157

Primavera, J.H., Lavilla-Pitogo, C.R., Ladja, J.M. & Dela Pena, M.R. (1993) A survey of chemical and biological products used in intensive shrimp farms in the Philippiness. *Marine Pollution Bulletin* 26: 35-40

Roth, M. (2000) The availability and use of chemotherapeutic sea lice control products. *Contributions to Zoology* 69(1/2): 109-118

Sorum, H. (1999) Antibiotic resistance in aquaculture. *Acta vet. Scand. Suppl.* 92: 29-36

Sorum, H. (2000) Farming of Atlantic salmon: an experience from Norway. *Acta vet. Scand. Suppl. 93*: 129-134

de Sousa, G., Fontaine, F., Pralavorio, M., Botta-Fridlund, D., Letreut, Y. & Rahmani, R. (1997) Insecticide cytotoxicity and CYP1A1/2 induction in primary human and rat hepatocyte cultures. *Toxicology in Vitro* 11: 451-457

Vivekanandhan, G., Savithamani, K., Hatha, A.A.M. & Lakshmanaperumalsamy, P. (2002) Antibiotic resistance of Aeromonas hydrophila isolated from marketed fish and prawn of South India. *International Journal of Food Microbiology* 76: 165– 168

Vonier, P.M., D.A. Crain, J.A. McLachlan, L.J. Guillette, Jr., and S.F. Arnold (1996). Interaction of environmental chemicals with the estrogen and progesterone receptors from the oviduct of the American Alligator. *Environmental Health Perspectives* 104(12): 1318-1322

Willis, C; Booth, H; Westacott, S; Hawtin P; (1999) Detection of antibacterial agents in warm water prawns. *Communicable Diseases and Public Health* 2(3): 210-214.

Xu, D., Grizzle, J.M., Rogers, W.A. & Santerre, C.R. (1996) Effect of cooking on residues of ormetoprim and sulfadimethoxine in the muscle of channel catfish. *Food Research International* 29(3-4): 339-344