Contributions to Zoology, 69 (1/2) 109-118 (2000)
SPB Academic Publishing bv, The Hague

The availability and use of chemotherapeutic sea lice control products

Myron Roth
Salmon Health Consortium, 907-75 Albert St., Ottawa, Canada, K1P 5E7; corresponding address: Aqua Health Ltd., 499 Clarence St. E. Ottawa, ON, Canada K1N 5S3

Keywords: sea lice, pesticide survey, chemotherapeutants

Abstract

An international survey revealed that eleven compounds representing five pesticide types are currently being used on commercial salmon farms for sea lice control. These include two organophosphates (dichlorvos and azamethiphos); three pyrethrin/pyrethroid compounds (pyrethrum, cypermethrin, deltamethrin); one oxidizing agent (hydrogen peroxide); three avermectins (ivermectin, emamectin and doramectin) and two benzoylphenyl ureas (teflubenzuron and diflubenzuron). The number of compounds available in any one country is highly variable, ranging from 9 (Norway) to 6 (Chile, United Kingdom) to 4 (Ireland, Faeroes, Canada) to 2 (US)). Dichlorvos, Azamethiphos and cypermethrin were the most widely used compounds (5 countries) followed by, hydrogen peroxide, ivermectin and emamectin (4 countries each), teflubenzuron (3 countries), diflubenzuron (2 countries), and deltamethrin, pyrethrum and doramectin (1 country each). Although, like trichlorfon, dichlorvos use is being discontinued in several countries notably Norway and the Faeroes. In most instances the availability of sea lice chemotherapeutants is limited, many being used under extra-label veterinary prescription or exemption, and special investigation permits. Access to a broad range of compounds with different modes of action, as well as application methods, has only recently been acquired making assessment of chemotherapy, and therefore integrated pest management, difficult.

Contents

Introduction

Clinical infestations of sea lice, *Lepeophtheirus salmonis* and *Caligus elongatus*, were first reported from salmon culture during the early 1970s in Norway following the development of systems for the intensive rearing of salmon in marine net-pens (Hastein and Bergsjo, 1976). Since then sea lice infestations have been reported from most, if not all, regions where salmon are farmed (Roth et al., 1993). In economic terms, sea lice outbreaks can be devastating. In 1996, annual costs associated with direct losses, treatment, and lost growth have been estimated at US $33.4 million (≈£20 million) in Norway (Kvenseth, 1997a), US $25 million (≈£15 million) in Scotland (Dear, 1997), and US $16 million (≈£10 million) in Canada (Roth, unpublished data).

Clinical outbreaks are managed through integrated pest management practices that incorporate fallowing and year class separation (Bron et al., 1993; Grant and Treasurer, 1993), the use of cleaner wrasse (Costello, 1993; Treasurer, 1993; Kvenseth, 1997b), good husbandry practices (Kvenseth, 1997a; Treasurer, 1998) and chemotherapy (Roth et al., 1993). While direct loss of stock from mortality and indirect losses from reduced growth represent the largest cost associated with sea lice infestations, they are both intricately linked to the cost and availability of chemotherapeutants used to man-

age outbreaks. Several chemotherapeutants have been developed for the control of sea lice, but specific details pertaining to clinical use practices vary from country to country. Roth et al. (1993) summarized information to date on sea lice chemotherapeutants, focusing largely on published and experimental data. This can be misleading from a practical perspective as the availability of specific compounds for clinical disease management may not be reported in the literature for commercial reasons, or may be reported but not in clinical use. In many instances, compounds which are not "approved" or licensed for specific use in salmon are used through other regulatory mechanisms. For example, in the US five drugs are approved for use in aquaculture, whereas approximately 20 "unapproved" compounds are used through investigational new animal drug (INAD) exemption and an additional 18 "unapproved" compounds, designated as low priority drugs, are also used (Schnick et al., 1997). Similar exemptions that allow investigational new drugs to be used exist in most regions where salmon are farmed. In addition, many therapeutants approved for use in other food animal species that are not specifically approved for use in salmon may be used through extra-label veterinary prescription (also referred to as "off-label" prescription, or "cascade procedures" (Europe)). Extra-label veterinary prescription is essential because real world conditions are always more variable than the limited options anticipated, investigated and reviewed during the regulatory approval process.

The availability of therapeutants affects the overall effectiveness of control in any particular region, through practical and competitive advantages gained by access to a large and variable range of chemotherapeutants. The purpose of the present study was to ascertain which compounds are currently in clinical use and to consider future development of sea lice control products.

Methods

An informal, confidential survey was distributed to fish health professionals with direct sea lice experience in the primary salmon farming countries. Only compounds approved for use in aquaculture, available through veterinary prescription, or otherwise legally available for clinical use were considered. Clinical use is defined as therapeutants administered to market fish (i.e., those harvested for human consumption). The term approved is used here to describe compounds that are fully approved, registered or otherwise licensed with specific label indications for the control of sea lice infections of farmed salmon or trout or other finfish in a given country.

Countries included in the survey were: Australia, Canada, Chile, Faeroe Islands, Japan, Iceland, Ireland, New Zealand, Norway, United Kingdom (UK)[1], and the United States (US). Data summarized pertains to 1997–1998 (early) therapeutant availability and treatment practices with some additional comments pertaining to availability in previous years.

Withdrawal times were not included in the general survey questions, but were reported by some respondents. In general, veterinarians prescribed withdrawal times as directed by label directions. However, as many compounds are used extra-label, prescribed withdrawal times may vary based on the attending veterinarian's professional judgement, sometimes being increased depending on circumstances (e.g. if a higher dose rate is used). Thus, the withdrawal times reported below do not cover all regions, or represent strict guidelines. They are reported here as an indicator of minima and maxima currently in clinical usage. Notation is given where withdrawal times varied with temperature.

Survey results

In total, 22 individuals were contracted from (# of respondents): Canada (4), Chile (3), Faeroes (1), Japan (3), Iceland (1), Ireland (2), Norway (2), UK (4)[1] and the US (2). As there are no therapeutants approved for sea lice treatment in Australia or New Zealand (see Schnick, 1997), and due to and absence of sea lice infestations in marine salmon cage culture, representatives from these regions were not contacted. The 22 respondents represented 12

[1]Scotland and Shetland Islands

(55%) veterinarians and 10 (45%) biologists. Affiliations for the groups included 9 (41%) private industry representatives[2], 8 (36%) government officials/researchers and 5 (23%) university researchers.

Eleven chemotherapeutants were reported to be in clinical use for the control of sea lice infections of farmed salmon. These compounds represent five classes, or types, of anti-parasitic agents: organophosphates, pyrethroids, oxidizers, avermectins and benzoylphenyl ureas. These can be further divided into topical (bath) chemotherapeutants and in-feed therapeutants. Few compounds reported are fully licensed or approved for use as sea lice control products. In most instances, therapeutants are obtained through extra-label veterinary prescription provisions or through investigational new drug applications/permits.

The results from the survey are summarized in Tables 1 and 2 and discussed below. Australia, Iceland, Japan and New Zealand have been omitted from Table 1 due to an absence of sea lice problems in salmon culture, and as such no compounds are reported to be in clinical use. Where relevant compounds are approved in these countries they are discussed below.

Organophosphates

Two compounds were reported to be used in several salmon farming countries: dichlorvos (Nuvan 500EC® & Aquagard SLT®, Novartis) and azamethiphos (Salmosan®, Novartis). Depending on the regulatory framework of the country in question, both compounds have been approved for sea lice control or used through extra-label veterinary prescription provisions/exemptions.

Trichlorfon (Neguvon®, Bayer) was not reported as being used in any country for sea lice control. The compound was previously licensed for use in Norway, but use has been discontinued since 1996. The compound is also licensed for use in Japan, but use is prohibited for sea water applications. The compound had also seen use in Chile, but has been displaced by more recently developed compounds.

Dichlorvos is currently used in the UK, Ireland and Chile (Table 1). The compound was previously extensively used in Norway, the Faeroe Islands and Iceland. In both Norway and the Faeroe Islands, dichlorvos use has been discontinued in favour of more recently developed therapeutants. Icelandic sea water production of salmon has been discontinued, eliminating the need for the chemical. Azamethiphos is in use in Norway, Faeroe Islands, Ireland and Canada where it approved for use in salmon. It is also licensed for use in the UK but cannot be used in Scotland without a discharge consent from the Scottish Environmental Protection Agency. However, since few discharge consents have been issued, azamethiphos use has been severely restricted.

Withdrawal times vary between compounds and countries. The reported withdrawal time for dichlorvos ranged from 4 (UK) to 14 d (Norway). The withdrawal time for azamethiphos ranged from 2 d (Canada) to 7 d (Norway) (Table 2).

Hydrogen peroxide

Hydrogen peroxide was reported to be used in 4 countries: Norway, the Faeroe Islands, the US, and the UK (Table 1). The compound is also licensed in Japan, but as sea lice are not problematic in sea water salmon culture use is directed towards fresh water applications. The compound was temporarily licensed for use on the East Coast of Canada during 1995 and 1996. Use was reported in Ireland during 1995, but has been discounted in favor of more recently developed compounds.

Formulations used were technical grade hydrogen peroxide solutions containing 50% w/v H_20_2 as supplied by industrial chemical manufactures (Azko Nobel, Interox, Air Liquid). Two preparations have been specifically approved for use in salmon: Salartect 500 FLT®, Brenntag; Paramove®, Solvay Interox.

Withdrawal times used range from 0 (Norway) to 1 day (UK, Canada) (Table 2).

[2]Figure includes veterinarians in private consultancy.

Table 1. Summary of Global Sea Lice Chemotherapeutants in Clinical Usage 1997/98

Country	Organophosphates		Pyrethrins & Pyrethroids			Oxidizers	Avermectins			Insect Growth Regulators		**Total** (in usage)
	Dichlorvos	Azamethiphos	Pyrethrum	Cypermethrin	Deltamethrin	H_2O_2	Ivermectin	Doramectin	Emamectin	Diflubenzuron	Teflubenzuron	
Norway												9
UK												6
Chile												6
Faeroes												4
Ireland												4
Canada												4
US												2
Total (in usage)	5	5	1	5	1	4	4	1	4	2	3	

Notes:
Norway & Faeroes: dichlorvos used in 1997 - discontinued in 1998.
Canada: pyrethrum and H_2O_2 temporarily registered on East Coast, registrations have now expired and not permitted for use.
Ireland: H_2O_2 use discontinued in 1998.
Japan: no requirement due to absence of lice problems, H_2O_2 is approved as a therapeutant
Iceland: no requirement due to absence of lice problems, dichlorvos is approved.
Australia & N. Zealand: no requirement due to absence of lice problems, no approved compounds

Table 2. Comparative Summary of Attributes of Sea Lice Chemotherapeutants

Chemotherapeutant	Therapeutic Dose	Toxic Dose (*Salmo salar*)	Therapeutic Margin	Withdrawal - Days (Country)[1]	Lice Stages Affected
Topical (Bath) Applications					
Dichlorvos	1.0 mg/L[2]	> 4.0 mg/L[2]	4x	4(UK), 14(N)	adult & pre-adult[3]
Azamethiphos	0.1 mg/L[4]	> 0.5 mg/L[5]	5x	2(C), 7(N)	adult & pre-adult[4]
Hydrogen Peroxide	1.5 g/L[6]	1.5 - 4.0 g/L[7,8]	0-3x	0(N), 1(UK,C)	adult & pre-adult-?[6,7,9]
Pyrethrum	10 µg/L - 10 g/L[10,11,12]	?	?	7(N), 30(C)	adult & pre-adult[10,11,12]
Cypermethrin	5.0 µg/L[13]	>0.5 mg/L[14]	100x	3(N,US)	adult & pre-adult[13]; larvae[15]
Deltamethrin	3.0 µg/L[16]	>10 µg/L[16]; (3.0 ug/L)[17]	0-3.5x	3(N)	adult & pre-adult[16]
In-Feed Application					
Ivermectin	0.2 mg/kg 1x[18] 0.02-0.2 mg/kg 1x-2x/wk, 9-40wk[19] 0.025 mg/kg, 2x/wk, 4 wk[20] 0.025 - 0.05 mg/kg, 2x/wk, 3wk[20] 0.07-0.08 mg/kg, 1x/wk, 3 wk[20]	0.4 mg/kg, 1x[18] 0.05 mg/kg /2d, 2wk[21]	2x ?	180(C) 1,000 dd[22] (C,UK)	adult, pre-adults & larvae[23]
Emamectin	0.05 mg/kg, 7d[24]	0.36 mg/kg, 7d[24]	7x	10 (C)[25]	adult, pre-adult & larvae[24]
Diflubenzuron	3 mg/kg - 14d[26]	N/A	N/A	60(N)	adult-?[27, 26], preadult & larvae[26]
Teflubenzuron	10 mg/kg - 7d[28]	N/A	N/A	21-42[29](C), 60(N)	adult-?[27, 28], pre-adult & larvae[28]

References/Notes: [1]Data from survey (see text for details): C=Canada, N=Norway, UK=United Kingdom, US=United States; [2]Horsberg et al., 1987; [3]Wooten et. al.,1982; [4]Roth et al., 1996; [5]Roth and Richards, 1992; [6]Treasurer and Grant, 1997; [7]Thomassen, 1993; [8]toxicity is temperature dependant: 1.5 g/l @ 18°C - 4.0 g/l @ 6°C [9]lice recovery following treatment noted; [10]Jakobson and Holm, 1990; [11]Boxaspen and Holm, 1991; [12]Hogans, 1994; [13]Hart et al., 1997; [14]Roth, unpublished data; [15]Fraser, 1995; [16]Alexandersen et al., 1997; [17]mortality noted at temperatures below 6°C; [18]Palmer et al., 1987; [19]Smith et al., 1993; [20]data from survey; [21]Johnson et al., 1993b; [22]degree days; [23]Johnson and Margolis, 1993; [24]SPAH, 1998; [2] Value authorized under Canadian Investigation New Drug submission; [26]Erdal et al., 1997; [27]reduced efficacy noted (see text); [28]Ritchie et al., 1997; [29]21d @ T>10°C, 42d @ T <10°C.

Pyrethroids

Pyrethroids, synthetic pyrethrin analogues, are increasingly being used in several salmon farming countries. The two principle compounds currently being used are cypermethrin (EXCIS®, Grampian Pharmaceuticals) and deltamethrin (Alpha Max®, Alpharma).

Five countries reported using cypermethrin including Norway, UK, Faeroes, Ireland and the US (Table 1). In all instances, cypermethrin has been made available to farmers through various regulatory mechanisms, principally through investigational new drug permits and exemptions. Deltamethrin was made available to Norwegian farmers as of 1998.

A withdrawal time of 3 days is currently used for both compounds in Norway and for cypermethrin in the US (Table 2).

Previously pyrethrum, a semi-synthetic natural extract of pyrethrin, (Py-Sal 25®, Norsk Pyrethrum A.S; SHC Pyrethrin Spray®, Salmon Health Consortium) was evaluated in several countries including Norway, Ireland and Canada, but has not been in widespread use. The compound is no longer in clinical use in Canada or Ireland. A limited amount was reported as being used in Norway, where a withdrawal time of 7 d was used (Table 2).

Avermectins

Ivermectin is the most widely used compound in this group, and was reported to be in use in four countries: Chile, Ireland, Canada and the UK (Table 1). While the compound is not specially approved for use in salmon, it is approved for a large number of other food production animal species and is therefore obtained through extra-label prescriptions in most countries, and can also be obtained over the counter from agricultural supplies distributors in others. Formulations used include the Ivomec® swine premix (0.6% a.i. dry powder), Ivome® injectable (1.0 % a.i. w/v injectable solution) or Oramec® drench (1.0 % emulsified concentrate) (all registrations to Merck, Sharpe and Dome Agvet).

A second compound from the avermectin group, emamectin benzoate (Slice®, Schering Plough Animal Health) is currently being developed specifically for use as a sea lice control product. The compound is currently being evaluated in clinical trials in Norway, Scotland, Chile, and Canada.

A related compound, doramectin (Dectomax®, Pfizer), was reported to be used in Chile under extra-label veterinary prescription.

Generally a withdrawal period of 1,000 degree days is used for ivermectin following treatment. In some regions, such as eastern Canada, a withdrawal period of 180 days is used regardless of water temperature (Table 2). As a result treatments with ivermectin are usually restricted to the first 12 months of sea water rearing to prevent conflicts with harvest schedules. A shorter withdrawal time of 10 days is approved for use in Canada for emamectin under an investigational new drug submission.

Benzoylphenyl ureas

Benzoylureas, commonly referred to as insect growth regulators, are the most recently developed group of sea lice chemotherapeutants targeted toward in feed application. Two compounds are currently in clinical usage for sea lice control: diflubenzuron (Lepsidon®, EWOS) and teflubenzuron (Ektobann®, Skretting; Calicide®, Trouw; Cal-X®, Moore Clark).

Diflubenzuron is currently in use in Norway and Chile. The compound was noted as being used in other countries such as the Faeroe Islands, but use was limited to a small number of field trials and no further information was provided with respect to further clinical use. Teflubenzuron was reported to be in use in Norway, Canada and Chile.

As with most drugs, withdrawal times vary from country to country. A withdrawal time of 60 days is currently in effect in Norway for both compounds. The withdrawal time for teflubenzuron in Canada is 21 days at water temperatures above 10°C and 42 days at water temperatures below 10°C (Table 2).

Discussion

This review summarizes the current availability of sea lice control chemotherapeutants from a clini-

cal perspective. Difficulties were encountered interpreting the results of the questionnaire due to the complexities defining what constitutes an "approved" compound and "clinical" use. In several countries, individual products were approved or pending approval. For the most part, many more compounds are used than are specifically approved for use to control sea lice in salmon through a variety legal means. This was especially true for cypermethrin, ivermectin, doramectin, emamectin, teflubenzuron and diflubenzuron. However, this situation should be viewed as a step-wise progression to full product approval as all these products, with the exception of ivermectin and doramectin, have been submitted for full product approval in several countries. Thus, the status of compounds in clinical usage in any given country is continually changing as new products are developed and evaluated.

Obtaining product approval in several countries is necessary in order for product sponsors to recover research, development and regulatory development costs. Ironically each additional country in which a new veterinary product submission is made increases product development cost significantly due to international differences in regulatory submission requirements. It is therefore not surprising to find that the largest number of compounds are approved (or pending approval) in Norway which represents the single largest market for sea lice compounds. Similarly, the number of products available to US salmon producers was found to be very low, largely due to small market size, but also due to significant differences that limit veterinary extra-label prescription privileges (Schnick and Armstrong, 1997).

Estimating the direct costs associated with compiling regulatory data requirements is very difficult, but costs can exceed several million dollars (Le Gouvello, 1997; Brackett and Roth, 1999). These costs can be very discouraging given the total market value for aquaculture therapeutants in any given country. For example the total sales of aquaculture therapeutants for all of Europe, including Norway, are estimated to be US $35 M per annum (≈£ 21 M) (Le Gouvello, 1997). In Canada, the market estimates of therapeutant sales for aquaculture are estimated to approximate CDN $3.5 M[3] (Roth, unpublished data). Thus, development costs may outweigh long term revenues. Cost centres include the cost for research and development, manufacturing quality control and increasingly stringent and complex environmental impact assessment studies (Brackett and Roth, 1999). This situation is further complicated where regulatory submission requirements are vague, indeterminate or interpreted on a case by case basis. For example, in the UK, azamethiphos has been approved by the Veterinary Products Committee, the agency responsible for reviewing data submissions, but lacks local discharge consent from local Scottish Environmental Protection Agency (Roth, 1998). As a result the compound is licensed, but usage is severely restricted.

Given the limited markets and the cost to develop aquaculture drugs, efforts to standardize testing requirements and to harmonize international regulatory submission requirements are critical to the future development of sea lice therapeutants. Efforts to harmonize registration efforts are underway in both Europe and North America (Schnick et al., 1997). However, therapeutant use may still be restricted by local legislation in some countries and/or regions which accounts for the variability observed in Table 1. This is particularly evident in the varying withdrawal times applied to therapeutants by different countries. Similar incongruities also exist when applying maximum residue limits, which if different can place unnecessary burdens on international trade of aquaculture products.

With the exception of doramectin (for which field data were unavailable at the time of writing), Table 2 lists the comparative attributes of the compounds reported in the survey. A comparison of the efficacies of the compounds reveals that each compound has advantages and disadvantages. Some, such as most of the topically applied compounds (bath treatments), are difficult to administer, not effective against all lice stages, but feature short withdrawal times. On the other hand, in-feed preparations have a wide efficacy range and allow farmers to treat many cages in a short period of time, provide a chemotherapeutic option in situations where

[3]Figure does not include vaccines.

tarpaulins would be impractical such as with large off shore systems, but feature longer withdrawal times. Thus, no one single compound is "ideally" suited for sea lice control (present summary; Costello, 1993; Roth et al., 1993). Longer withdrawal times are often applied to in-feed chemotherapeutants in current usage to comply with "zero" residue tolerance requirements when compounds are used off-label, or under investigation new drug permits. As these compounds are assessed and characterised from a pharmacological, human safety and environmental impact perspective, it is likely that the difference between withdrawal times of bath treatments and in-feed treatments will become less pronounced.

Respondents to the questionnaire noted that chemotherapy practices varied with the production cycle, in-feed treatments being used in the first year of production and topical treatments being used in the second year. However, several countries have lacked a suitable range compounds to employ such treatment strategies. For example, in Norway organophosphates represented the sole class of compound available to farmers until 1994 when hydrogen peroxide and pyrethrin became available (Grave et al., 1991; Kvenseth, 1997a). Neither of these latter compounds, however, are effective against larval lice (Johnson et al., 1993a; Hogans, 1994). Compounds effective against larval lice, such as the insect growth regulators (Erdal et al., 1997; Ritchie et al., 1997) only became available in 1996. A similar situation has existed in Scotland for some time resulting in an over dependance on the use of dichlorvos that led to the development of resistance in some populations of lice (Jones et al., 1992). In Canada, farmers have had access to ivermectin for several years, but not to compounds with short withdrawal times until the recent approval of hydrogen peroxide and azamethiphos. As a result, it is hypothesized that outbreaks of sea lice have persisted, or increased due to limited access to an appropriate range of chemotherapeutants necessary for the development of effective integrated pest management strategies.

While access to an increasing number of therapeutants will undoubtedly contribute to better lice management, questions remain. From a lice management perspective, in-feed treatments are significant in that they are efficacious against a wider range of lice life stages thus reducing the need for repeat treatments. This in turn should reduce the overall amount of compound used, maximizing drug efficiency and reducing potential problems associated with resistence. However, many respondents noted that in the case of ivermectin, fish are treated over a several month period during the first sea summer (see also Smith et al., 1993). This would appear to suggest that the infectious challenge is very intense over the summer months, or efficacy is sub-optimal for unknown reasons. A similar therapeutic approach is taken with the application of benzoylphenyl ureas. However, in the case of the latter compounds, efficacy against adult lice is known to be reduced (Erdal et al., 1997; Ritchie et al., 1997)[4], thereby reinforcing the need to optimize treatment timing and necessitating repeat treatments. Interestingly, despite repeated use ivermectin for several years in Ireland no evidence has been reported suggesting the selection of resistance.

Given the recent availability of a range of chemotherapeutants, many with different modes of action, close attention to strategic use of chemotherapeutants will be required to accurately assess the effectiveness of chemotherapy and ensure the long term usefulness of the limited number of available treatment compounds.

Acknowledgements

The author wishes to thank all those contacted during the survey for sharing their wisdom, experiences and comments.

References

Alexandersen S, Midttun B, Martinsen B. 1997. ALPHA MAX™, a novel deltamethrin formulation for treatment of sea lice on Atlantic salmon (*Salmo salar*). Abstract, *8th International Conference, Diseases of Fish and Shellfish, Eur. Assoc. Fish Pathol.* Edinburgh 1997: 0-57.

Boxaspen K, Holm JC. 1991. A new treatment against sea lice. *EAS Spec. Publ.* **14**: 36-37.

Brackett J, Roth M. 1999. The economics of approval and registration of therapeutants for aquaculture. *Salmon Health*

[4]Adult lice do not molt and reductions in numbers are most likely due to recruitment failure rather than acute toxicity.

Report '99, Northern Aquaculture Special Edition, Febr. 1999: 6-8.

Bron JE, Sommerville C, Wootten R, Rae GH. 1993. Fallowing of marine Atlantic salmon, *Salmo salar* L. farms as a method for the control of sea lice, *Lepeophtheirus salmonis* (Krøyer, 1837). *J. Fish Diseases* **16**: 487-493.

Costello MJ. 1993. Review of methods to control sea lice (Caligidae: Crustacea) infestations on salmon (*Salmo salar*) farms. In: Boxshall GA, Defaye D, eds. *Pathogens of wild and farmed fish: sea lice.* Chichester: Ellis Horwood, 219-252.

Dear G. 1997. A fish farmers perspective of the significance of disease. *Presentation, 8th International Conference "Disease of Fish and Shellfish", Eur. Assoc. Fish Pathol.* Edinburgh 1997.

Erdal JI, Toneby M, Rønningen K, Wallace C. 1997. Clinical field trials with diflubenzuron medicated pellet for treatment of Atlantic salmon (*Salmo salar*, Linné) against salmon lice (*Lepeophtheirus salmonis* Krøyer). Abstract, *8th International Conference "Disease of Fish and Shellfish", Eur. Assoc. Fish Pathol.* Edinburgh 1997: 0-59.

Fraser NR. 1995. Effect of cypermethrin formulated as GPRD01 on chalimus stages of sea lice infecting Atlantic salmon (*Salmo salar*) at a sea water temperature of 7.5°C. *Report prepared for Grampian pharmaceuticals limited, Research Division, Lancashire, UK.*

Grant AN, Treasurer JW. 1993. The effects of fallowing on caligid infestations on farmed Atlantic salmon (*Salmo salar* L.) in Scotland. In: Boxshall GA, Defaye D, eds. *Pathogens of wild and farmed fish: sea lice.* Chichester: Ellis Horwood, 256-260.

Grave K, Engelstad M, Soli NE. 1991. Utilization of dichlorvos and trichlorfon in salmon farming in Norway during 1981-1988. *Acta Veterinaria Scandinavica* **32**: 1-7.

Hart JL, Thacker JRM, Braidwood JC, Fraser NR, Mattews JE. 1997. Novel cypermethrin formulation for the control of sea lice on salmon (*Salmo salar). Veterinary Record* **140**: 179-181.

Hastein T, Bergsjo T. 1976. The salmon lice *Lepeophtheirus salmonis* as the cause of disease in farmed salmonids. *Riv. Ital. Pisc. Ittiopatlogia* **11**: 3-5.

Hogans WE. 1994. Efficacy of the Salmon Health Consortium Pyrethrin Spray for the treatment of sea lice (*Caligus elongatus*) on cultured Atlantic salmon (*Salmo salar*) in marine waters of the Lower Bay of Fundy. *Report prepared for the Salmon Health Consortium, Ottawa, Canada*: 4 pp.

Horsberg TE, Derge GN, Høy T, Djupvik HO, Hogstad IM, Hektoen H, Ringstad R. 1987. Diklorovs som avlusningsmiddel for fisk. Kilinisk utprøving op toksisitetstesting. (Dichlorvos as a fish delousing agent. Clinical trials and toxicity testing). *Norsk veterinærtidsskrift* **99**: 611-615.

Jakobsen PJ, Holm JC. 1990. Promising tests with new compound against sea lice. *Norsk Fiskeoppdrett* Jan: 16-18.

Johnson SC, Constible JM, Richard J. 1993a. Laboratory investigations on the efficacy of hydrogen peroxide against the salmon louse *Lepeophtheirus salmonis* and its toxicological and histopathological effects on Atlantic salmon *Salmo salar* and chinook salmon *Oncorhynchus tshawytscha. Diseases of aquatic organisms* **17**: 197-204.

Johnson SC, Kent ML, Whitaker DJ, Margolis L. 1993b. Toxicity and pathological effects of orally administered ivermectin in Atlantic, chinook, and coho salmon and steelhead trout. *Diseases of Aquatic Organisms* **17**: 107-112.

Johnson SC, Margolis L. 1993. Efficacy of ivermectin for control of the salmon louse *Lepeophtheirus salmonis* on Atlantic salmon. *Diseases of Aquatic Organisms* **17**: 101-105.

Jones MW, Sommerville C, Wootten R. 1997. Reduced sensitivity of the salmon louse, *Lepeophtheirus salmonis* to the organophosphate dichlorvos. *Journal of Fish Diseases* 15: 197-202.

Kvenseth PG. 1997a. Best current practice for lice control in Norway. *Caligus* **2**: 4-9.

Kvenseth PG. 1997b. Lice fighting the environmentally friendly way! *Caligus* **2**: 11-12.

Le Gouvello R. 1997. Models of partnership for registration of drugs and vaccines for aquaculture. *Presentation, 8th International Conference "Disease of Fish and Shellfish", Eur. Assoc. Fish Pathol.* Edinburgh 1997.

Palmer R, Rodger H, Drinan E, Dwyer C, Smith PR. 1987. Preliminary trials on the efficacy of ivermectin against parasitic copepods of Atlantic salmon. *Bull. Europ. Assoc. Fish Pathol.* **7**: 47-54.

Ritchie G, Hoff KA, Rønsberg SS Isdahl E, Adriolo EMH. 1997. The efficacy and use of oral teflubenzuron in an integrated control strategy for the treatment of sea lice (*Lepeophtheirus salmonis*) infestations of farmed Atlantic salmon (*Salmo salar*). *Abstract, 8th International Conference "Disease of Fish and Shellfish", Eur. Assoc. Fish Pathol.* Edinburgh 1997.

Roth M. 1998. Aquaculture therapeutant registration in the United Kingdom. *Salmon Health Report '98, Northern Aquaculture Special Edition,* March 1998: 14-15.

Roth M, Richards RH. 1992. Trials on the efficacy of azamethiphos an its safety to salmon for the control of sea lice. In: Michel C, Alderman DJ, eds. *Chemotherapy in Aquaculture: from Theory to Reality.* Paris: Office International Des Epizooties, 212-218.

Roth M, Richards RH, Dobson DP, Rae GH. 1996. Field trials on the efficacy of the organophosphate azamethiphos for the control of sea lice (Copepoda: Caligidae) infestations of fared Atlantic salmon (*Salmo salar*). *Aquaculture* **140**: 217-239.

Roth M, Richards RH, Sommerville C. 1993. Current practices in the chemotherapeutic control of sea lice infestations in aquaculture: a review. *Journal of Fish Diseases* **16**: 1-26.

Schering Plough Animal Health (1998). SLICE® Technical Monograph. Schering Plough Animal Health, Union, New Jersey: 0-32.

Schnick RA, Armstrong R. 1997. Aquaculture drug approval

progress in the United States. *Salmon Health Report, A Northern Aquaculture Supplement* Jan. 1997: 22-28.

Schnick RA, Alderman DJ, Armstrong R, Le Gouvello R, Ishihara S, Lacierda EC, Percival S, Roth M. 1997. World wide aquaculture drug and vaccine registration progress. *Bull. Europ. Assoc. Fish Pathol.* **17**: 251-260.

Smith PR, Moloney M, McElligott A, Clarke S, Palmer R, O'Kelly J, O'Brien F. 1993. The efficiency of oral ivermectin in the control of sea lice infestations of farmed Atlantic salmon. In: Boxshall GA, Defaye D, eds. *Pathogens of wild and farmed fish: sea lice.* Chichester: Ellis Horwood, 296-307.

Thomassen JM. 1993. Hydrogen peroxide as a delousing agent for Atlantic salmon In: Boxshall GA, Defaye D, eds. *Pathogens of wild and farmed fish: sea lice.* Chichester: Ellis Horwood, 290-295.

Treasurer JW. 1993. Management of sea lice (Caligidae) with wrasse (Labridae) on Atlantic salmon (*Salmo salar* L.) farms. In: Boxshall GA, Defaye D, eds. *Pathogens of wild and farmed fish: sea lice.* Chichester: Ellis Horwood, 335-345.

Treasurer JW. 1998. Sea lice management methods in Scotland. *Caligus* **5**: 8-12.

Treasurer JW, Grant A. 1997. The efficacy of hydrogen peroxide for the treatment of farmed Atlantic salmon, *Salmo salar* L. infested with sea lice (Copepoda: Caligidae). *Aquaculture* **148**: 265-275.

Wootten R, Smith JW, Needham EA. 1987. Aspects of the biology of the parasitic *Lepeophtheirus salmonis* and *Caligus elongatus* on farmed salmonids, and their treatment. *Proc. Royal Soc.* Edinburgh **81B**: 185-197.

Received: 18 March 1999