



Salmon Health

20th FLOOR, 45 O'CONNOR STREET
OTTAWA, ONTARIO, K1P 1A4
Phone (613) 788-6851 Fax (613) 235-7012

August 27, 1997

0957 '97 AUG 29 P3:43

New Brunswick
Salmon Growers
Association

British Columbia
Salmon Farmers
Association

Aquaculture
Association of
Nova Scotia

Ontario Aquaculture
Association

Maine Aquaculture
Association

Moore-Clark Co.
(Canada) Inc.

ALPHARMA Inc.

Brenntag (UK) Ltd.

Microtek
International Ltd.

Eka Chemicals Inc.

Shur-Gain -
A member of Maple
Leaf Foods Inc.

Syndel
Laboratories Ltd.

Heritage
Aquaculture Ltd.

Schering-Plough
Animal Health

Atlantic Fish
Health Inc.

Pfizer Canada Inc.

National Research
Council- Institute for
Marine Biosciences

Nova Scotia
Department
of Fisheries

PEI Department of
Environment
& Fisheries

Dockets Management Branch (HFA-305)
Food and Drug Administration
12420 Parklawn Drive, Room 1-23
Rockville, MD 20857

Dear Colleagues,

RE: Comments on development of options to encourage animal drug approvals for minor species and for minor uses.

Docket No. 97N-0217

Salmon Health, a self-funding, non-profit program of the Canadian Aquaculture Industry Alliance, was established to ensure that fish culturists have access to safe and effective fish health management tools in an appropriate regulatory environment. Salmon Health is responding to this request for comments because:

- Salmon Health receives support from the Maine Aquaculture Association
- The United States is a key export market for Canadian farmed salmon
- Salmon Health has five years of experience working to address this particular issue in Canada, a country with a comparable drug regulatory system to the United States. Solutions in one country are likely to be transferrable to the other.

Approved drugs for managing minor species production health problems are very important, and the issue is consistently at the top of fish producers' concerns. Salmon Health congratulates the Food and Drug Administration for initiating an effort to develop legislative and regulatory steps in response to this need. The ability to manage production animal health is key because it ensures animal production industry growth and development.

97N-0217

J
C 6

The following comments on progressive minor use legislative and regulatory changes are organized according to the format provided in the request for comments published in Docket No 97N-0217.

A. Scope

The criteria found at Sec 514.1 (d) (1) are satisfactory.

B. Creating Additional Statutory Authority

It is very important that human safety standards for minor use drugs do not differ from those for major food animal species drugs because minor species food animal producers need to ensure continued consumer confidence in their products. A critical corollary is that consumers must also be confident that imported food animal products have clearly been managed and treated with the same degree of care given to domestically grown food products.

One recommended change advisable for human safety standards would be to simplify producers for the extrapolation of residue depletion data between related minor species by allowing the use of pivotal studies that provide safe limits to withdrawal periods rather than exact residue depletion times. This is particularly applicable to poikilotherms, for example, if a drug has a 45 day withdrawal period in salmon, then the residue depletion component of a label extension to catfish should be satisfied by a study that demonstrates that catfish are also residue free at 45 days, rather than a complete residue depletion analysis in catfish. Crop grouping is a valid approach but may require considerable study before it can be implemented.

Target species safety and efficacy standards should be allowed to differ from those required for major species drugs. A valuable new improvement would be to remove the requirement for Good Laboratory Practices for pivotal target animal safety and efficacy studies, if the study is supervised, funded or conducted by a national producer association for a minor species. The members of this association have a vested interest in ensuring that these studies are conducted legitimately and these associations should be permitted the opportunity to take on this responsibility. GLP requirements should be

maintained for sponsor funded and conducted studies, independent of national producer organization review. This producer association should clearly be a national organization of all producers with a vested interest in the safe use of the drug.

Conditional approvals and post market surveillance are not an ideal option for obtaining additional approvals, unless these procedures are adopted for both minor and major species. Otherwise the distinctions in regulatory requirements may discourage manufacturers familiar with the major species requirements from sponsoring minor use products.

Acceptance of the results of foreign reviews would be a very beneficial action in support of minor species approvals. The challenge that minor species face is that regulatory costs exceed market sales estimates. Accepting foreign reviews will effectively increase the market while holding regulatory costs constant, and provide CVM with improved access to a world wide body of scientific knowledge on animal drugs approved in other countries. Therefore this change will help to ensure that minor use sponsors come forward and approvals are subsequently obtained. The acceptability of foreign reviews should be based on bilateral equivalency agreements between regulatory agencies, not by assessment of reviews for individual products. Government regulatory agency reviews are more likely to maintain consumer confidence than reviews by private organizations. Additionally using expert panels for reviews is not an ideal approach, although this option may be of value in deciding whether to assess low regulatory priority status for a particular drug.

C. Administrative and Regulatory Changes

Manufacturing standards should be the same for approved drugs for minor and major species to ensure consumer confidence is maintained.

D. Creating Incentives

The creation of economic incentives to encourage manufacturers to sponsor minor use drugs is a critical step. The problem is widely recognized to be that

the minor use drug market is too limited to recoup the regulatory costs of entry. Tax breaks for supporting manufacturers are an excellent approach. The extra revenues returned to the nation from the economic growth of food animal production industries could compensate for, or exceed, revenues lost through concessions to drug manufacturers. Grants to producers' associations to support products that address industry priorities are also an appropriate step. However, the producer association must be a national organization and include all producers likely to benefit from use of the product under the proposed label claim. This will reduce the possibility that relatively limited resources could be divided between competing products. Periods of market exclusivity for minor use products are also a positive incentive for manufacturers. There may be concern that this will lead to overly inflated prices; however, in reality the manufacturer has to ensure the product is available at a price that will sell. These incentives are most appropriate for minor use drugs for food animal production, rather than companion animal drugs, given the need to ensure that human safety issues are fully addressed for food animal treatments, and the greater option for off label treatment of companion animals using injectable formulations. The NRSP-7 funding program should not extend its mandate to include additional species.

The creation and support of Public Master Files is not an ideal approach. The approval process requires data on a specific formulation, which is difficult to address through a Public Master File. A manufacturer may have a considerable file of data on a differing formulation and find that the Public Master File does not reduce regulatory costs significantly. Support for Minor Use Drugs will be more successful if public revenues are used to ensure that economic incentives are in place to bring manufacturers forward as sponsors for their particular formulation. One issue to consider would be the linkage of economic incentives to a requirement that a manufacturer keep a supported product on the market for at least some minimum time period (five years, for example) following regulatory approval.

One critical point to address is to ensure that the manufacturer can be absolutely certain that sponsorship of a minor use label claim will have no negative impact on the other label claims for major species. Any concern that there will be potential negative impact on major use claims is an extremely

strong disincentive to support minor use species approvals.

Salmon Health agrees with the suggestion in the Request for Comments material that philanthropic and not-for-profit organizations should be encouraged to support minor species drug approval research.

E. Extending Existing Legal Authority

Extending current legislation to allow extra label prescriptions for in-feed drug use and production uses eg spawning hormones in fish will encourage minor species drug approvals. Extra label drug prescriptions help to demonstrate to manufacturers the market for a particular drug. Additionally, the process encourages producers to work with veterinary fish health professionals, thereby improving the medical care of production fish and ensuring that a medically trained expert is involved in the drug use decision making process. Extra label use of drugs in feed, compared to any other route of administration, is not likely to present a greater human safety risk through increasing the probability of residues in subsequent food products. Given the residue problems that have been encountered with injection sites, it is possible that the reverse is true.

Thank you for the opportunity to provide these comments.

Sincerely

A handwritten signature in black ink, appearing to read "Rob Armstrong". The signature is fluid and cursive, with the first name "Rob" being more prominent and the last name "Armstrong" following in a similar style.

Rob Armstrong
Executive Director



Salmon Health

20th FLOOR, 45 O'CONNOR STREET
OTTAWA, ONTARIO, K1P 1A4
Phone (613) 788-6851 Fax (613) 235-7012
August 27, 1997

New Brunswick
Salmon Growers
Association

British Columbia
Salmon Farmers
Association

Aquaculture
Association of
Nova Scotia

Ontario Aquaculture
Association

Maine Aquaculture
Association

Moore-Clark Co.
(Canada) Inc.

ALPHARMA Inc.

Brenntag (UK) Ltd.

Microtek
International Ltd.

Eka Chemicals Inc.

Shur-Gain -
A member of Maple
Leaf Foods inc.

Syndel
Laboratories Ltd.

Heritage
Aquaculture Ltd.

Schering-Plough
Animal Health

Atlantic Fish
Health Inc.

Pfizer Canada Inc.

National Research
Council Institute for
Marine Biosciences

Nova Scotia
Department
of Fisheries

PEI Department of
Environment
& Fisheries

Dockets Management Branch (HFA-305)
Food and Drug Administration
12420 Parklawn Drive, Room 1-23
Rockville, MD 20857

Dear Colleagues,

RE: Comments on development of options to encourage animal drug approvals for minor species and for minor uses.

Docket No. 97N-0217

Salmon Health, a self-funding, non-profit program of the Canadian Aquaculture Industry Alliance, was established to ensure that fish culturists have access to safe and effective fish health management tools in an appropriate regulatory environment. Salmon Health is responding to this request for comments because:

- Salmon Health receives support from the Maine Aquaculture Association
- The United States is a key export market for Canadian farmed salmon
- Salmon Health has five years of experience working to address this particular issue in Canada, a country with a comparable drug regulatory system to the United States. Solutions in one country are likely to be transferrable to the other.

Approved drugs for managing minor species production health problems are very important, and the issue is consistently at the top of fish producers' concerns. Salmon Health congratulates the Food and Drug Administration for initiating an effort to develop legislative and regulatory steps in response to this need. The ability to manage production animal health is key because it ensures animal production industry growth and development.

The following comments on progressive minor use legislative and regulatory changes are organized according to the format provided in the request for comments published in Docket No 97N-0217.

A. Scope

The criteria found at Sec 514.1 (d) (1) are satisfactory.

B. Creating Additional Statutory Authority

It is very important that human safety standards for minor use drugs do not differ from those for major food animal species drugs because minor species food animal producers need to ensure continued consumer confidence in their products. A critical corollary is that consumers must also be confident that imported food animal products have clearly been managed and treated with the same degree of care given to domestically grown food products.

One recommended change advisable for human safety standards would be to simplify producers for the extrapolation of residue depletion data between related minor species by allowing the use of pivotal studies that provide safe limits to withdrawal periods rather than exact residue depletion times. This is particularly applicable to poikilotherms, for example, if a drug has a 45 day withdrawal period in salmon, then the residue depletion component of a label extension to catfish should be satisfied by a study that demonstrates that catfish are also residue free at 45 days, rather than a complete residue depletion analysis in catfish. Crop grouping is a valid approach but may require considerable study before it can be implemented.

Target species safety and efficacy standards should be allowed to differ from those required for major species drugs. A valuable new improvement would be to remove the requirement for Good Laboratory Practices for pivotal target animal safety and efficacy studies, if the study is supervised, funded or conducted by a national producer association for a minor species. The members of this association have a vested interest in ensuring that these studies are conducted legitimately and these associations should be permitted the opportunity to take on this responsibility. GLP requirements should be

maintained for sponsor funded and conducted studies, independent of national producer organization review. This producer association should clearly be a national organization of all producers with a vested interest in the safe use of the drug.

Conditional approvals and post market surveillance are not an ideal option for obtaining additional approvals, unless these procedures are adopted for both minor and major species. Otherwise the distinctions in regulatory requirements may discourage manufacturers familiar with the major species requirements from sponsoring minor use products.

Acceptance of the results of foreign reviews would be a very beneficial action in support of minor species approvals. The challenge that minor species face is that regulatory costs exceed market sales estimates. Accepting foreign reviews will effectively increase the market while holding regulatory costs constant, and provide CVM with improved access to a world wide body of scientific knowledge on animal drugs approved in other countries. Therefore this change will help to ensure that minor use sponsors come forward and approvals are subsequently obtained. The acceptability of foreign reviews should be based on bilateral equivalency agreements between regulatory agencies, not by assessment of reviews for individual products. Government regulatory agency reviews are more likely to maintain consumer confidence than reviews by private organizations. Additionally using expert panels for reviews is not an ideal approach, although this option may be of value in deciding whether to assess low regulatory priority status for a particular drug.

C. Administrative and Regulatory Changes

Manufacturing standards should be the same for approved drugs for minor and major species to ensure consumer confidence is maintained.

D. Creating Incentives

The creation of economic incentives to encourage manufacturers to sponsor minor use drugs is a critical step. The problem is widely recognized to be that

the minor use drug market is too limited to recoup the regulatory costs of entry. Tax breaks for supporting manufacturers are an excellent approach. The extra revenues returned to the nation from the economic growth of food animal production industries could compensate for, or exceed, revenues lost through concessions to drug manufacturers. Grants to producers' associations to support products that address industry priorities are also an appropriate step. However, the producer association must be a national organization and include all producers likely to benefit from use of the product under the proposed label claim. This will reduce the possibility that relatively limited resources could be divided between competing products. Periods of market exclusivity for minor use products are also a positive incentive for manufacturers. There may be concern that this will lead to overly inflated prices; however, in reality the manufacturer has to ensure the product is available at a price that will sell. These incentives are most appropriate for minor use drugs for food animal production, rather than companion animal drugs, given the need to ensure that human safety issues are fully addressed for food animal treatments, and the greater option for off label treatment of companion animals using injectable formulations. The NRSP-7 funding program should not extend its mandate to include additional species.

The creation and support of Public Master Files is not an ideal approach. The approval process requires data on a specific formulation, which is difficult to address through a Public Master File. A manufacturer may have a considerable file of data on a differing formulation and find that the Public Master File does not reduce regulatory costs significantly. Support for Minor Use Drugs will be more successful if public revenues are used to ensure that economic incentives are in place to bring manufacturers forward as sponsors for their particular formulation. One issue to consider would be the linkage of economic incentives to a requirement that a manufacturer keep a supported product on the market for at least some minimum time period (five years, for example) following regulatory approval.

One critical point to address is to ensure that the manufacturer can be absolutely certain that sponsorship of a minor use label claim will have no negative impact on the other label claims for major species. Any concern that there will be potential negative impact on major use claims is an extremely

strong disincentive to support minor use species approvals.

Salmon Health agrees with the suggestion in the Request for Comments material that philanthropic and not-for-profit organizations should be encouraged to support minor species drug approval research.

E. Extending Existing Legal Authority

Extending current legislation to allow extra label prescriptions for in-feed drug use and production uses eg spawning hormones in fish will encourage minor species drug approvals. Extra label drug prescriptions help to demonstrate to manufacturers the market for a particular drug. Additionally, the process encourages producers to work with veterinary fish health professionals, thereby improving the medical care of production fish and ensuring that a medically trained expert is involved in the drug use decision making process. Extra label use of drugs in feed, compared to any other route of administration, is not likely to present a greater human safety risk through increasing the probability of residues in subsequent food products. Given the residue problems that have been encountered with injection sites, it is possible that the reverse is true.

Thank you for the opportunity to provide these comments.

Sincerely

A handwritten signature in black ink, appearing to read "Rob Armstrong". The signature is fluid and cursive, with a long, sweeping tail on the final letter.

Rob Armstrong
Executive Director



Salmon Health
20th Floor, 45 O'Connor Street
Ottawa, Ontario, CANADA
K1P 1A4



Dockets Management Branch (HFA-305)
Food and Drug Administration
12420 Parklawn Drive, Room 1-23
Rockville, MD 20857