

THE 2002 PROPOSED FOREST PROTECTION PROGRAM

AGAINST THE BALSAM FIR SAWFLY

USING AERIALLY APPLIED BOTANICAL INSECTICIDE

NEEMIX 4.5 (azadirachtin)

Submission to:

**Department of Environment
Environmental Assessment Division**

by:

**Department of Forest Resources and Agrifoods
NEWFOUNDLAND FOREST SERVICE**

March 2002

NAME AND ADDRESS OF PROPOSER

This application is submitted on behalf of

**THE DEPARTMENT OF FOREST RESOURCES & AGRIFOODS
NEWFOUNDLAND FOREST SERVICE
ST. JOHN'S, NF**

Chief Executive Officer:

Mr. Allan Masters

Deputy Minister

729-4720

St. John's

Contact Person:

Mr. Hubert Crummey

Supervisor, Forest Insect and Disease Control

637-2424

Corner Brook

THE UNDERTAKING:

In fulfilment of the mandate and commitment of the Department of Forest Resources & Agrifoods to protect the forest resource and limit damage from infestations of significant pests, with due regard for human health and non-target environmental effects, the following undertaking is proposed.

NATURE OF PROPOSED PESTICIDE APPLICATION

The Province is still faced with a serious infestation of the balsam fir sawfly. This infestation is threatening the substantial investment in silviculture and consequently the long term wood supply for the forest industry. The Department of Forest Resources and Agrifoods is proposing to carry out a limited operational aerial control program to selected forest areas (mainly silviculturally treated stands) to address the sawfly problem. The control program will focus on areas in western and southern Newfoundland forecast to receive moderate and severe balsam fir sawfly defoliation in 2002

PURPOSE OF PROPOSED PESTICIDE APPLICATION

Background:

Coniferous defoliators are natural elements in the forests of Newfoundland and Labrador. The need to protect the forest resource against insects has been seen in terms of past outbreaks of hemlock looper and spruce budworm. The potential impact of unchecked forest pest outbreaks cannot be ignored. In the 1970s, a major infestation of spruce budworm occurred. Due to the lack of early intervention to control the budworm, (full scale, adequate programs were only initiated in 1978 and 1981 which were very late in the outbreak), it was estimated that the

Province suffered tree mortality of up to 50 million m³ of balsam fir and black spruce. This equates to about a 25 year wood supply for the entire forest industry based on current demand.

The 1980 Royal Commission on Forest Protection and Management confirmed the magnitude of the existing budworm problem and recommended that Government adopt a long-term policy on protection, particularly related to investment in expensive silvicultural practice aimed at renewing the forest resource. This recommendation, along with many others, was adopted by Government and provided the basis for forest spraying policy within the Province. Control programs since 1980 have become an integral part of forest management, with particular emphasis being placed on protecting silviculture areas. To date, the position of the Department is that the forest resource will be protected against insect pests, using the most effective federally registered pesticides which have the least impact on the environment. It is imperative that a variety of control tools / methods be available to allow for efficient and effective control of pest infestations as the situation arises. No particular tool / method works well in all situations. In addition, the Department is committed to actively seek more acceptable solutions to pest problems, such as: biological insecticides, enhancing natural control measures or any other practical methods of pest management. All pesticide usage is subject to annual environmental assessment and/or review processes within the Province, as deemed necessary. Annually, Government decides on the nature and extent of a program based on all available information and recommendations.

Without such a protection policy, the Royal Commission recommended that silvicultural prescriptions not be undertaken. As silviculture efforts continue to increase, the need to protect these substantial investments in forest management against losses to insects and diseases becomes more apparent. A future wood supply for the forest industry is dependent on a vigorous, healthy, growing stock, which can reach rotation age relatively free from significant insect and disease infestations. Also a healthy forest is equally important for ecosystem management, biodiversity and environmental health.

The Province has been reasonably successful in the past in dealing with major forest insect pests such as the spruce budworm and hemlock looper where treatment was adequate. Previous control programs have limited the potential impacts of insect infestations by minimizing extensive tree mortality and saving as much foliage as possible. The balsam fir sawfly, usually a minor insect pest, is at this time defoliating forest stands and in particular pre-commercial thinning areas and younger second growth areas. Pest management intervention is required. The Province and the pulp and paper industry (Corner Brook Pulp & Paper Ltd. and Abitibi-Consolidated Inc.) have invested over \$150 million into silviculture in these areas over the last 20 years and cannot afford to lose them through mortality or through ongoing growth loss from insect defoliation. The balsam fir sawfly is threatening this investment and pest management measures are necessary.

Current situation:

The proposed pest management program has been developed to address the balsam fir sawfly

problem in western and southern Newfoundland and to maximize protection of valuable young stands and silviculturally treated areas where treatment is applied. The purpose of the program is to reduce insect population levels of the sawfly during the larval feeding stages in treated areas and thereby minimize the loss of foliage, the loss of tree growth and to prevent potential tree mortality which could result from trees weakened by insect attack. This will help preserve growth and the substantial dollar investment made in establishing these areas to intensively manage the forest.

Control options:

Because the sawfly historically has not been a major problem up to now, the Department only has very limited options to deal with the situation. Research and experimental programs were carried out in 1998, 1999, 2000, and 2001 in Newfoundland and in other jurisdictions to develop acceptable biological control options for a number of sawflies, principally the balsam fir sawfly and the yellowheaded spruce sawfly. Progress has been made on a number of potential biological controls and work will continue.

The common biological insecticide that has been applied aerially in forests against the spruce budworm and hemlock looper, *Bacillus thuringiensis* var. *kurstaki* (B.t.k.), is not effective against sawflies. B.t.k. was isolated from, and developed into a control product for, certain pest insects belonging to the Order Lepidoptera (the butterfly and moth group). Sawflies belong to the Order Hymenoptera, a different group. In order for B.t.k. to be effective, it must be ingested and the protein crystal and spore component of the product must encounter the right

conditions in the insect gut. The lining of the insect midgut must have the appropriate receptor sites for the B.t.k. toxin to bind and thereby do its work. It appears that sawfly larvae are not susceptible to B.t.k. as are the budworm or looper. Other strains of the biological insecticide(B.t.), *Bacillus thuringiensis* var. *israelensis* (B.t.i.), registered for control of mosquito and black fly larvae and applied to water systems have been looked at in terms of potential development for use against the sawfly groups, but none has shown great promise to date. The search continues.

Also in 1999, 2000 and in 2001, the naturally occurring balsam fir sawfly virus (NeabNPV) was tested experimentally on small areas. NPV viruses are usually host (insect) specific or some affect related sawflies. In fact several NPV viruses are registered for control of their specific host insect. The results from these trials were favourable and further testing is proposed for 2002. A separate submission will be prepared by the Canadian Forest Service, the research agency conducting this work.

In 1999, the botanical insecticide Neemix 4.5 (azadirachtin), one part of the extract from the seed of the Neem tree (*Azadirachta indica*) found in India and parts of Africa, was tested on balsam fir sawfly in Nova Scotia and on yellowheaded spruce sawfly in both Newfoundland and Nova Scotia. The results were very encouraging for both insects. Based on previous limited trials with Neem insecticide (azadirachtin) on balsam fir sawfly and the 1999 data, the manufacturer of one azadirachtin product (Neemix 4.5) applied to Health Canada - Pest Management Regulatory Agency (PMRA) for a registration of their product for control of both of these sawflies, as well

as another sawfly in Ontario.

Proposed control product - Neemix 4.5:

Neemix 4.5 (azadirachtin) is a naturally occurring botanical insecticide. It has a number of properties which affect target pests, including insecticidal, insect growth regulator and an anti-feedant, depending on the rate applied. The main mode of action occurs when the insect eats foliage treated with the product. It stops feeding, is unable to molt successfully, and dies in 4 - 7 days. Azadirachtin insecticides are registered for use in many countries including the USA and effective against more than 300 pest species in forestry, agriculture, home garden, storage of grains, and urban pests. Neem insecticides are widely used for pest control in organic farming on crops such as lettuce, tomatoes and potatoes. In the USA, it is used for indoor and outdoor use. It is registered for aerial and/or ground application to horticultural and ornamental plants, trees, shrubs, and agricultural crops. Neemix 4.5 is effective against sawflies such as the balsam fir sawfly, the yellowheaded spruce sawfly and the pine false webworm. Health Canada - Pest Management Regulatory Agency gave Neemix 4.5 a Temporary Registration in 2000 and again 2001. In 2001, approximately 1,500 ha were treated in Bay d'Espoir to evaluate the product operationally. Sawfly larval numbers were reduced in treated areas, but there were some problems with the formulation in terms of compatibility with spray equipment. This is being resolved by the manufacturer. It is anticipated that the Temporary Registration will be renewed in 2002. [see attachment to document].

Neemix 4.5 breaks down very rapidly in the environment by sunlight and water action

(hydrolysis). One-half of the product reaching the foliage, soil and litter is broken down in 24 to 48 hours. In the USA, the federal regulatory agency (Environmental Protection Agency) has not put restrictions on food products because of the rapid break down.

Neemix 4.5 is effective, relatively safe to non-target organisms, readily disappears from the environment and is acceptable. It has low acute toxicity. It is practically non-toxic to mammals, birds and rats. Neemix is relatively harmless to natural insect enemies and has minimal risk for honeybees and other pollinators. Although toxic to rainbow fish and the water flea, use at the proposed rate, the interception of the spray by the forest, and the use of required buffer zones, means that there is low risk to these organisms from its use. The model used by PMRA to determine buffer zones indicated that none were necessary. However, as an additional safety margin, a 50 meter buffer zone is required around aquatic resources.

Neemix has a wide margin of safety for both users and consumers. Although irritating to the eye and skin, particularly for workers, the use of protective equipment during handling will result in very little, if any, effect. If the eye or skin is contacted, flushing of the eye with clean water or rinsing the skin with soap and water is all that is required.

Neemix does not buildup in animals and therefore, it is safe to eat fish and game animals from treatment areas as the amount that might be present in the meat would be negligible. Because Neemix degrades so rapidly, there will be no risk of berry contamination at picking time.

Previous to this current product, the only

other pest control option that was used successfully (in 1998 and 1999 for balsam fir sawfly and in 1998 for yellowheaded spruce sawfly), where application could occur, was the chemical insecticide Dylox. However, due to large buffer (no spray) zones around designated areas, it was not possible to adequately deal with the pest problem. Dylox is not a consideration in 2002. The Department is moving away from traditional insecticides where there are effective and efficient alternatives.

DESCRIPTION OF UNDERTAKING

Insect Population Levels

The balsam fir sawfly is a native insect and occasionally a common pest on balsam fir in Newfoundland. It has become more important as a pest of young and semi-mature balsam fir, particularly in thinned stands. The population overwinters in the egg stage in fir needles and larvae usually hatch around mid-July (depending upon seasonal development influenced by weather) and feed on the previous year and older foliage for a number of weeks before pupating. Adult sawflies emerge in August, mate and eggs are laid in the needles of the current year. Populations have been regulated by natural parasites and predators. Outbreaks have occurred every 3 or 4 years, in various places. Past epidemics of this insect have been of short duration (3 or 4 years) and were terminated by natural factors, including a natural occurring viral (nuclear polyhedrosis virus - NPV) disease. Although localized damage was often severe, tree mortality was limited. However, defoliation also caused and is causing significant growth loss to affected trees and weakening them, making them susceptible to other mortality factors. Research by the Canadian Forest Service has

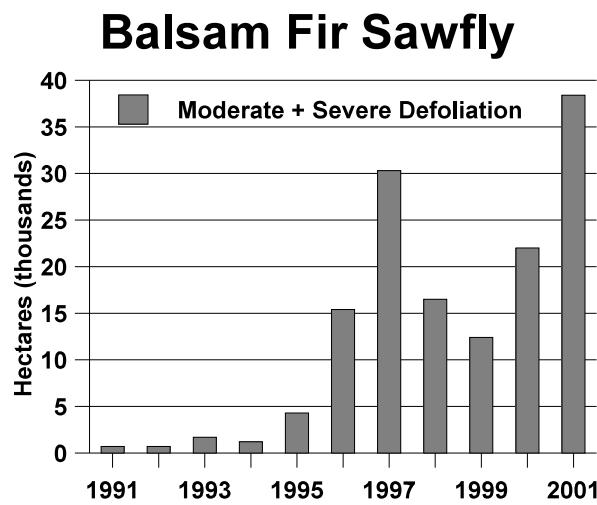
indicated that, based on growth prior to sawfly defoliation and expected future growth, that at two study sites, after defoliation has ceased, there may be from 13 -18 years of reduced growth before the trees recover to pre-infested growth rates.

The current infestation in western Newfoundland was detected in 1991 near Bottom Brook, east of Stephenville. The following figure summarizes the moderate and severe defoliation history in western NF, where the largest infestation is occurring. Other infestations have occurred on the Burin Peninsula, and the one in Bay d'Espoir appears to be declining.

The balsam fir sawfly infestation has and continues to expand and move northward and northeastward into previously unaffected areas, mainly thinned stands. In 2000, the infestation on the Burin Peninsula actually decreased and is expected to continue to decline. The infestation in Bay d'Espoir

needles. In the first year of infestation with moderate and severe defoliation, all but the current growth turns a blasty orange color and is quite visible. In the subsequent year, because only the needles of the previous year remain on the branches and provide food for the sawfly larvae, the damaged needles do not show up as readily and therefore may not be mapped, although there is moderate and severe defoliation present.

The 2002 moderate and severe balsam fir sawfly defoliation forecast is for a total of approximately 65,500 ha to be affected. In western NF, approximately 57,400 ha are forecast extending from south of Grand Lake north to Old Mans Pond and from Stag Lake-Cooks Brook across the Humber Arm near Gillams and eastward to Steady Brook-Corner Brook Lake. This is a significant increase in the infestation in western NF. In Bay d'Espoir, 8,100 ha are forecast for moderate and severe defoliation extending from Morrisville to Jeddore Lake and from Medonngonix Lake north to Bernard Brook-Twillick Pond. This infestation appears to be breaking up. The locations of the insect infestations (damage) predicted for 2002 as well as the general locations of potential treatment areas under consideration are as indicated on the accompanying maps. These areas are not treatment block boundaries. Spray blocks will be identified later, subject to the necessary "no-spray" buffer zones and other stipulations, as dictated by the Department of Environment. The continuing expansion of the infestation in western NF is cause for concern in that more silviculture areas are going to be affected. In excess of 10,000 ha of pre-commercial thinnings (PCTs) are infested at present. These PCTs have been established, at an



had affected most of the fir by 2000 and in 2001, there were signs of some decline. It should be noted that it is very difficult to map cumulative annual moderate and severe defoliation. The sawflies feed on all age class needles except the current year's

average cost in excess of \$1,000 per hectare (a total amount in excess of \$ 10 million), to enhance growth and are critical to maintaining an adequate wood supply for the forest industry. The impact of this infestation, if left unchecked, will be the loss of this substantial investment. The failure to adequately protect the investment in silviculture, and the potential loss of future harvestable stands, would be significant to both the social and economic well being of the people, particularly on the west coast of the Island, both in terms of direct as well as indirect employment and in spin-off economics.

As indicated by the forecast, it does not appear that any significant natural factors are influencing this population. These infested and defoliated trees are not growing. They are barely surviving. They have reduced vigour, are under considerable stress, and are susceptible to other significant factors including mortality from secondary insects and diseases. It is estimated that, since the outbreak began, the Province has lost in excess of 2 m³ of growth per hectare infested per year. This equates to the loss of in excess of 120,000 m³ of incremental growth during this infestation.

Balsam Fir Sawfly Control Activity

Health Canada - Pest Management Regulatory Agency (PMRA) has given Neemix 4.5 a detailed review in terms of the current information available on this product and granted Neemix 4.5 a Temporary Registration for 2001. It is anticipated that this will continue in 2002. A registration authorizes its use against the specified insect(s) subject to specific conditions and stipulations which ensure the health and safety of the public and the environment. More specific information about Neemix is attached to this

document.

Based on the forecast, a significant area is expected to be affected in 2002, much of which has been silviculturally treated. The Department is proposing to operationally treat up to approximately 3,000 ha in western NF and Bay d'Espoir with this botanical insecticide, subject to the resolution of the formulation problems identified in 2001, and subject to the renewal of the Temporary Registration from Health Canada-Pest Management Regulatory Agency. **Treatment areas will be refined as environmental concerns, e.g. buffer zones, are determined and stipulated in the Operator Licence.**

As per the product label authorized by Health Canada - Pest Management Regulatory Agency, 20 - 50 grams of active ingredient are permissible per hectare in a single treatment. The Department is proposing to apply approximately 25 g a.i. per hectare. The final dosage will be determined in consultation with Provincial regulatory officials.

An Operators Licence from the Department of Environment will be requested to allow use of Neemix 4.5 in 2002.

It is anticipated that the products will be applied to selected sites within the forecast by single engine spray aircraft.

Treatment is expected to start in July, however, it could be in late June (depending on weather affecting insect hatching and development) and continue into early August. Operations on the

west coast would be based out of the Stephenville or Deer Lake Airports and out of the airstrip at Bay d'Espoir for that part of the program. Final aircraft type that could be used will depend on aircraft availability, operational parameters, economics, logistics, and final spray block sizes. The Department uses the most up-to-date technology to ensure the best delivery of the program.

numbers from early in the season, to determine the ideal application date(s) and priorities of areas to be treated. Monitoring to determine insecticide efficacy continues throughout the spray program, and the final assessment is made after insect feeding has ended. All necessary ground, communication and sampling equipment is supplied and owned by the Department.

UNDERTAKING PARAMETERS

SPRAY PROCEDURES

Since 1977, the Forest Protection Division of the Newfoundland Department of Forestry & Agriculture (now the Forest Engineering & Industry Services Division of the Department of Forest Resources & Agrifoods) assumed responsibility for any control programs conducted against forest insect and disease pests and to date have planned and supervised major insect control programs. The insect population forecast, now carried out by Departmental staff, predicts infestation levels for the following summer and this is used to determine if there is a need for control intervention and if so, provides the outline to identify proposed treatment areas. The Department has carried out all other aspects of the operational aerial programs (apart from the actual aircraft application of the insecticide and aircraft maintenance), including the transportation, handling, mixing, loading and decontamination of equipment and containers, up to and including the loading of aircraft. The Department also oversees the actual spraying by the contractor to ensure that the proper areas are treated under the appropriate weather conditions, and that all Licence stipulations, including buffer zones, are followed. The Department monitors insect and host tree shoot development and larval

The Department utilizes currently available equipment and technology. It complies with existing regulatory guidelines. In earlier programs navigation of spray aircraft was provided by utilizing qualified and licenced Departmental personnel. Usually a supervisor, in a helicopter, led spray aircraft along pre-determined flight lines, and a supervisor, in a fixed-wing aircraft or a helicopter, determined the accuracy of the navigation and performance of the spray aircraft, and initiated corrective action, as necessary. The supervisor also assessed the favourability of weather parameters before and during spray missions. As in 1998, 1999, 2000 and 2001, because of the buffer zones stipulated in the provincial Operators Licence, the Department required the use of Differential Global Positioning System (DGPS). This system of navigation enabled the spray aircraft pilots and aerial supervisors to better anticipate identified buffer zones during spray missions and also to facilitate the actual flight along the pre-determined flight lines. The system has worked reasonably well. This technology is the best available at this time for operational programs. This system is proposed for use in 2002. The aerial supervisor is still monitoring and directing the treatment as well as assessing the accuracy of the application and the suitability of weather, etc, as before.

Spray bases have been provided with appropriate equipment to ensure environmental safety by using approved containment dyking and currently acceptable safety and emergency equipment and materials.

WORKER SAFETY

The Department has well-established safety guidelines for workers involved in insect control activity. Staff have a lot of experience and an enviable safety record. To protect workers involved with the programs, personnel handling the insecticide (each mixer/loader) will be required to wear hooded rubber suits, rubber gloves, rubber boots, goggles and appropriate respirators during the mixing of the insecticide formulation, the filling of loading and holding tanks and aircraft, and during the decontamination of insecticide drums (as per current occupational health and safety standards and product label instructions). Pilots and navigators/supervisors are not permitted to be involved in the handling of insecticides.

In addition, approved safety precautions and established rules and guidelines will be adhered to concerning personal hygiene of all mixer/loader personnel working with insecticides and what to do if contact with an insecticide occurs or if symptoms of illness occur during or after handling of any insecticide or mix. Hospital and emergency telephone numbers will also be posted in a conspicuous place to be used in the event of accident.

Applicable contingency measures will be available to personnel in the event of an accident.

PUBLIC HEALTH CONSIDERATIONS

To minimize the risk of exposure of people to insecticide spray, "no-spray" buffer zones will be left around known places of permanent human habitation and around areas such as cabin development and park camp and day use areas. In 2002, spraying near habitation will be subject to terms and conditions of the Operator's Licence from the Department of Environment in consultation with the appropriate Health and Community Services personnel. Cabins will be adequately buffered in relation to the product being applied. In addition, a 1.6 km buffer zone is left around identifiable intakes to known community water supplies; however, it may be desirable to decrease buffers in specific cases. These are dealt with in consultation with the provincial Department of Environment on an individual basis as and when identified. If, during the course of a spray mission, unauthorized personnel are detected in or near a treatment area, the aerial supervisor will instruct the spray aircraft pilot(s) to provide extra buffers or to terminate the mission, as applicable in the circumstance. Local hospitals and regional public health officials in the vicinity of the proposed spray areas are notified in advance of the program concerning which product(s) are to be used, general areas of treatment blocks, timing of spray season, etc. This action is to ensure full notification and preparation should an incident occur which would require medical assistance.

ENVIRONMENTAL SAFETY

In terms of environmental safety, all stipulations in the licence issued by the provincial

Department of Environment are followed. These include the reporting of any incidents, such as spills, to the appropriate authorities. In connection with this, the Department of Forest Resources and Agrifoods has a contingency plan which is annually reviewed and approved prior to receiving of an Operator's Licence. The plan outlines procedures for spill reporting, emergency first aid for exposure, insecticide spill only, aircraft crash in bush, aircraft accident on or near the airport, jettisoned aircraft load, drum decontamination and disposal, and other general regulations and instructions as necessary.

PUBLIC NOTIFICATION

As part of the program, the public and media in the vicinity of the proposed treatment areas are notified, prior to commencement of the program, through ads or news releases, or through appropriate contact if required, with information of which product is being used, general areas of spray blocks, timing of application, contact numbers, etc. Access roads to the general areas are posted with signs indicating treatment, product, dates, and phone numbers for more information. A phone-in information line will be set up and the general public can call to find out the status of areas receiving treatment. Since 1977, daily messages have been sent to the news media with information indicating what areas are ready to be treated as well as the status of areas which have been treated since the last update.

Regional offices of the Department of Forest Resources & Agrifoods and the Department of Environment, as applicable, will be provided with maps showing treatment blocks. These maps are available for viewing by the general public during regular office hours. District offices of the

Department will be made aware of spray blocks in their area and are provided with applicable detailed maps so they can inform the public on specific local blocks, when requested.

POTENTIAL SPRAY CONFLICTS:

There are always potential conflicts with insect control programs. Such factors as proximity to habitation, cabin development areas, individual cabins, water supply areas, recreational uses (fishing and camping, berry picking), potential impacts on wildlife. However, in approving a product at the federal registration level, and in granting a licence at the provincial level, mitigating measures are identified which eliminate or significantly reduce the potential for conflicts. These mitigating measures are outlined on the product label as approved by the PMRA-Health Canada and in terms of buffer zones stipulated in the Operator's Licence [**see attachments to this document**]. In addition, the proponent is also required to post signs and advise the public about the program to lessen accidental exposure.

ALTERNATE OPTIONS FOR SAWFLY CONTROL

Integrated Pest Management Approach

The Department prefers, and has been actively encouraging and participating in research focussed on the identification and development of, biological solutions to insect problems. This work will continue. Another potential biological control option has been / is being pursued. The naturally occurring balsam fir sawfly virus will be tested again in 2002. The Canadian Forest Service has

requested a research permit from PMRA and will apply to the provincial Department of Environment for the necessary licenses and permits. Scientists will continue to look at alternate and more acceptable solutions.

In terms of a biological approach, which is a longer-term option, to the major problem with balsam fir sawfly but also the yellowheaded spruce sawfly, in 1997 a cooperative research agreement involving the Canadian Forest Service, Corner Brook Pulp and Paper Ltd. and Abitibi-Consolidated Inc. was initiated investigating the ecology of the balsam fir sawfly in terms of natural control factors such as viruses, fungi and parasites to try and determine what, if any, of these are present in the population and why natural factors have not affected these sawfly populations to date. In addition, the impact of both sawflies, particularly the balsam fir sawfly and any differences between thinned and unthinned stands which may be causing this particular outbreak to expand without any obvious natural controls, was being investigated. This research continued in 1998 with Canadian Forest Service (CFS) and continued in 1999, 2000 and 2001 with additional resources available from an NSERC grant obtained by the University of New Brunswick and involving CFS personnel as well. This cooperative research agreement, in identifying what natural factors are influencing these populations and what biological or other more acceptable means could be used to limit tree damage during outbreaks, could lead to additional integrated pest management solutions. Progress is being made with this research in terms of sawfly population study, natural sawfly virus development and impacts of the sawflies on host trees. A final report is expected in 2002.

Also, in attempting to improve control

measures and techniques, the Canadian Forest Service, in cooperation with the Department and the Forest Industry, will continue to identify methods of dealing with pest outbreaks. Experimental programs are an integral part of operational programs and essential to better manage pest problems in an effective and efficient manner.

The Department of Forest Resources & Agrifoods will continue to explore control options (and field test promising candidates) for insect pests to determine cost effective, efficient control methods with regard to minimizing human health risks and environmental impacts.

APPROVAL OF THE UNDERTAKING

Aerial (and ground) application of insecticides falls under both federal and provincial legislation. The approval of product use (operationally or experimentally) has first to be given by the federal government. This mandate rests with the Pest Management Regulatory Agency of Health Canada.

In Canada, before they are registered, pesticides must have undergone extensive assessments for both environmental impact and human health risks, when used according to label directions under appropriate weather conditions.

In Newfoundland, pesticide application has to be carried out under an Operators Licence, issued by the Department of Environment, and under the direction of qualified and licenced Applicators.

The Federal Government, insecticide

manufacturers, universities and colleges are also involved in pesticide research. Decisions, made by government after all of the research has been reviewed, are made with wide safety margins.

Any manufacturer who wishes to sell a pesticide in Canada must first register that pesticide under the *Pest Control Products (PCP) Act*. To receive registration, the manufacturer must follow the registration process administered by the Pest Management Regulatory Agency (PMRA) of Health Canada. Registration involves the submission of an application by the manufacturer. Before this is possible, the company must carry out specific studies on the product. The application must be supported by a very thorough data package documenting the effects of the pesticide on users, bystanders and the environment.

The scientific testing may take years, depending on the nature of the product, as the study includes long and short term health effects of the user, exposure to bystanders, residues in food, ground water contamination, effects on wildlife and environmental fate. A scientific evaluation of the product is then performed by Health Canada. A registration will be granted if the pesticide's safety, merit and value for the proposed use are found to be acceptable. If problems with the product are identified, registration will not be granted. All products are subject to re-evaluation, with provision for suspension or cancellation.

Once the federal government approves a registration, the provincial governments become more involved. Each province has legislation dealing specifically with pesticide use in that province. In

Newfoundland and Labrador pesticide use is regulated under the *Pesticides Control Act*. This legislation requires all organizations and companies using pesticides to apply for and receive a Pesticide Operator License. This license regulates aspects of an operation not covered by federal legislation and requirements. As with federal regulations, the Pesticide Operator License is designed to minimize risks to human health and the environment. Aspects of a pesticide operation like buffer zones, spill response, public information and notification programs, monitoring requirements, weather conditions, etc are all specified in the license as they relate to a particular spray program.

Provincial legislation also requires individuals to be trained in the safe use of pesticides. Only individuals that successfully pass the provincial pesticide applicator exam (administered by the Department of Environment - Pesticides Control Section) are granted an applicator license and authorized to handle pesticides. Compliance and enforcement activities are also carried out by the Pesticides Control Section.

As with all commercial pesticide operations, the 2002 insecticide program will be regulated by the Pesticides Control Section of the Department of Environment [**see attachments to this document**]. The Federal registration system combined with the provincial licensing and regulatory system ensures that any pesticide that is used in Canada has passed a comprehensive environment/health evaluation.

SCHEDULE

The insects will emerge, and the best time

for application of control, is expected to be early July to late July, but weather dependent. Because of the logistics and acquisition of supplies and services, it is essential that approval be given at the earliest.

HEALTH CANADA - PMRA
DOCUMENT ON NEEMIX 4.5

See Appendix C

Also attached is the Neemix 4.5 label

March 27, 2002 Original signed by

Date Allan Masters
 Deputy Minister

ATTACHMENTS

MAPS OF INFESTED AREAS PREDICTED FOR
2002

see Appendix A

COPY OF 2001 OPERATORS LICENCE (TERMS
AND CONDITIONS) FROM THE DEPARTMENT of
Environment APPLICABLE TO FOREST
INSECTICIDE USE

see Appendix B

Appendix A

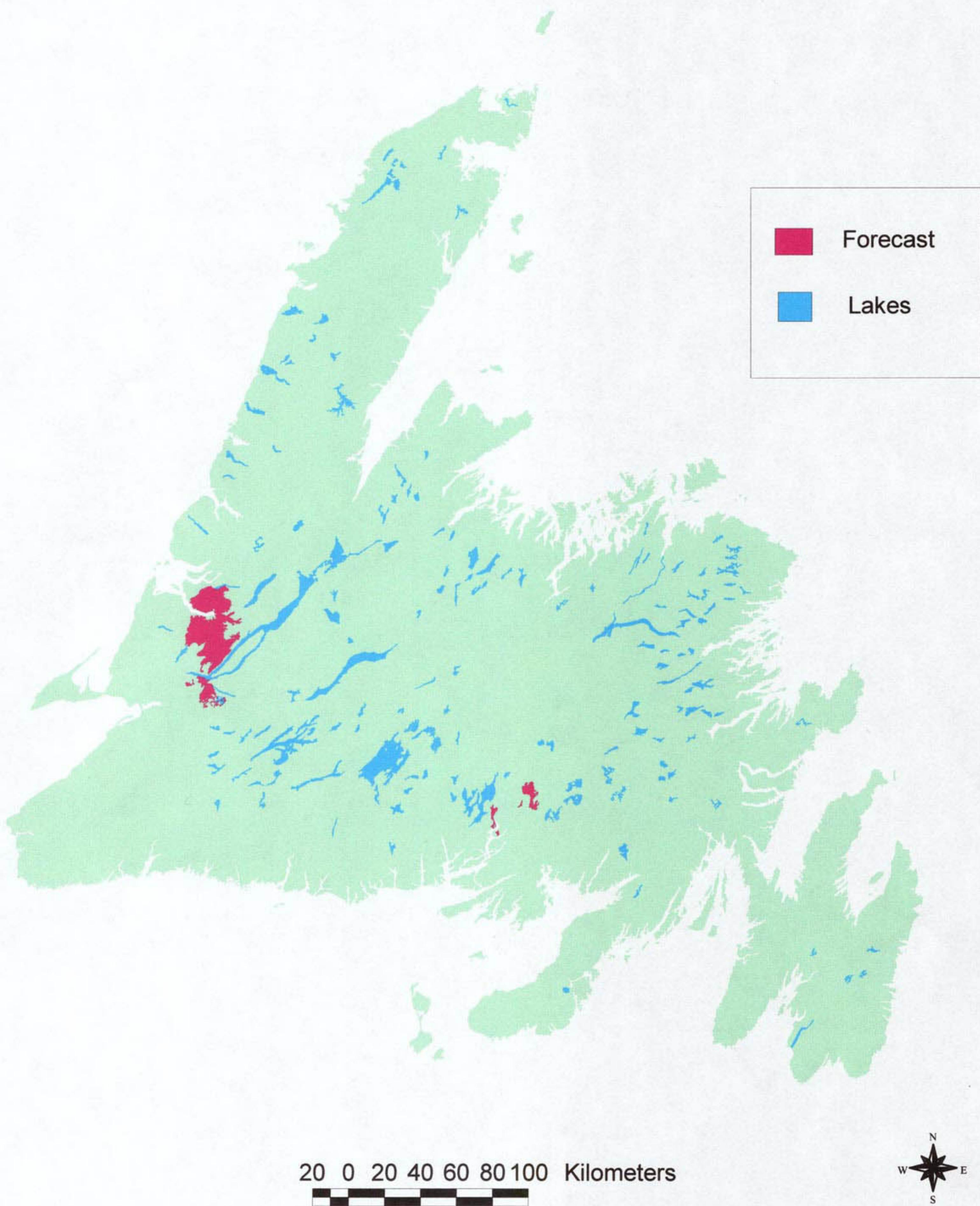
- 1) Map of Insular Newfoundland showing general infestation areas
- 2) Maps of **Infested** areas **Predicted** for 2002 where treatment may occur

NOTE:

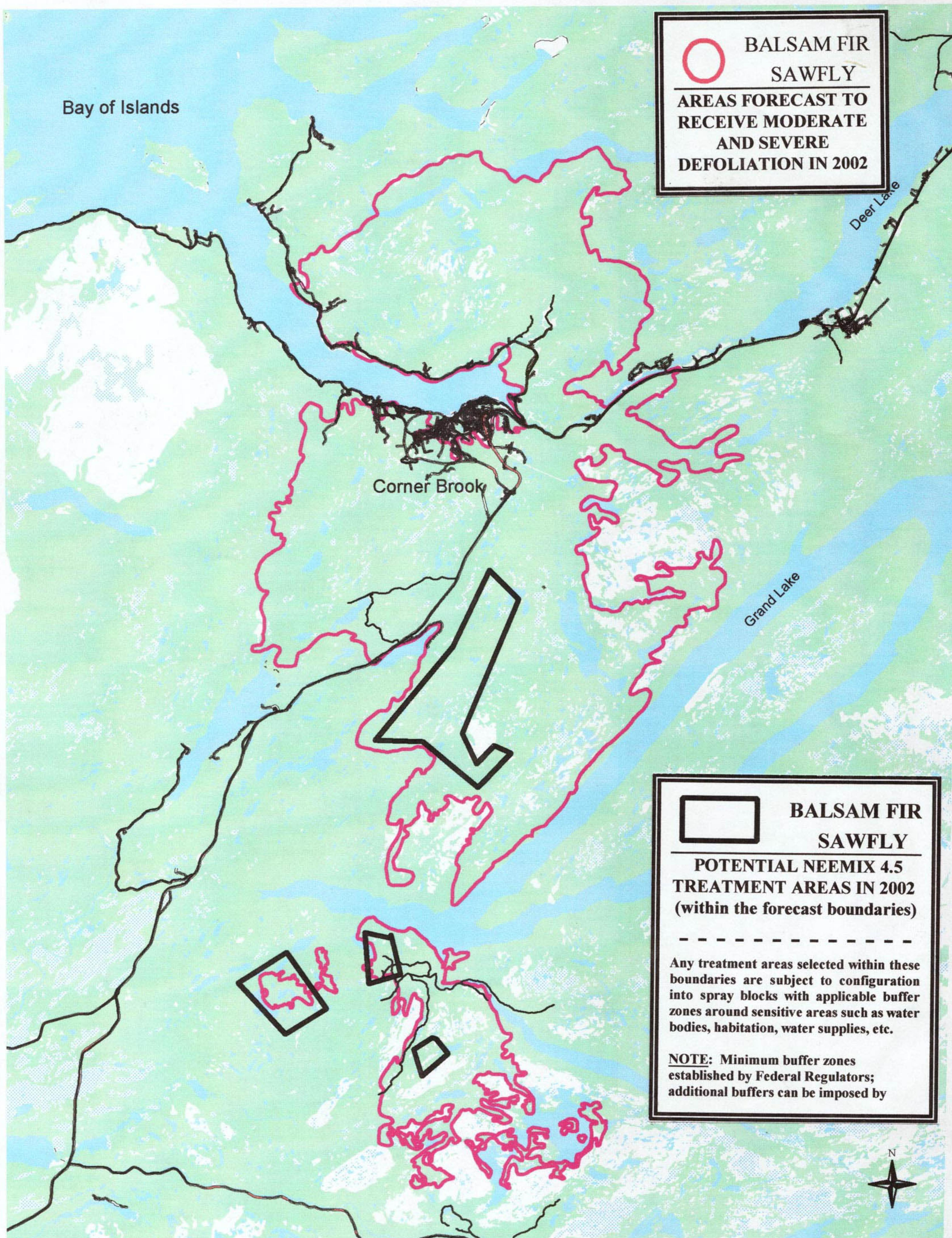
The areas outlined on the following maps indicate where the sawfly populations and expected defoliation / damage will occur in 2002. They are not final treatment areas. Spray (treatment) blocks will be established within these boundaries once the terms and conditions and buffer zones (no-spray areas) are determined by the provincial Department of Environment under the approval and licensing process.

2002 Balsam Fir Sawfly Forecast

Moderate & Severe Defoliation



2002 Balsam Fir Sawfly Forecast (Western)



2002 Balsam Fir Sawfly Forecast (Bay d'Espoir)

 **BALSAM FIR
SAWFLY**
**AREAS FORECAST TO
RECEIVE MODERATE
AND SEVERE
DEFOLIATION IN 2002**

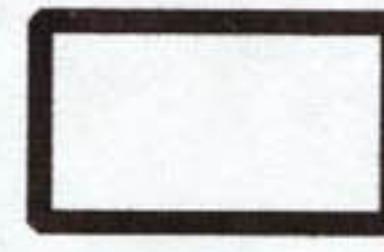
Jeddore Lake

Head of
Bay d'Espoir

St. Alban's

Conne River

Scale 1: 200,000

 **BALSAM FIR
SAWFLY**

**POTENTIAL NEEMIX 4.5
TREATMENT AREAS IN 2002
(within the forecast boundaries)**

Any treatment areas selected within these boundaries are subject to configuration into spray blocks with applicable buffer zones around sensitive areas such as water bodies, habitation, water supplies, etc.

NOTE: Minimum buffer zones established by Federal Regulators; additional buffers can be imposed by

Appendix B

Copy of 2001 Pesticide Operators Licence (modified to show only the applicable sections pertaining to forest insecticide application)

GOVERNMENT OF
NEWFOUNDLAND AND LABRADOR

**Department of
Environment**

Pesticides Control Section

PESTICIDE OPERATOR LICENCE

TERMS AND CONDITIONS

DEPARTMENT OF FOREST RESOURCES AND AGRIFOODS

June 2001

1. **Definitions**

Waterbody: means any surface (high water mark) or subterranean source of fresh or salt water within the province, whether such course usually contains water or not, and includes coastal water within the jurisdiction of the province and includes water above the bed of the sea that is within the jurisdiction of the province, any river, stream, brook, creek, water course, lake, pond, spring, lagoon, ravine, gully, canal and any other flowing or standing water and the land usually or at the time covered by any such body of water.

Well: means an artificial opening in the ground from which water is obtained or that is made for the purpose of exploring for or obtaining water.

Human habitation: means every structure in which a person or persons resides on either a part-time or full time basis.

2. For the purpose of this licence, all definitions and regulations as indicated in the Pesticides Control Act, RSN 1990, c. P-8 and the Pesticides Control Regulations, 1166/96 shall apply.
3. All applications shall be conducted in strict compliance with the label registered under the authority of the Pest Control Products Act (Canada).
4. The operator shall be limited to using only those pesticides and applicators as indicated on its Pesticide Operators License Application dated June 21, 2001. Any changes in the program outlined in the application must receive written approval of the Manager, Pesticides Control Section, prior to their implementation.
5. The operator shall review these terms and conditions with each applicator prior to the start of each season, and a copy of the terms and conditions shall be provided to each applicator.
6. A copy of the operators licence and these terms and conditions shall be available at each site during the application of a pesticide. In addition, the operator shall ensure that all applicators have their applicators license in their possession while applying pesticides.
7. Upon completion of the pesticide program for the year, the operator shall submit to the Pesticides Control Section details regarding the type and quantity of each pesticide used and the name of the vendor(s) from whom the pesticide was purchased. This information shall be submitted no later than December 31 of each year. Licenses for the following season will not be processed until this information is received.
8. Empty pesticide containers which have been triple rinsed, cleaned and rendered unusable may be disposed off at an Approved waste disposal site. Contaminated material shall be disposed off in accordance with the manufacturer's directions and in consultation with the Pesticides Control Section.
9. All spills involving greater than 10 liters of mixed pesticide or the equivalent of unmixed formulation shall be reported immediately. All spills involving mixed or unmixed pesticide into a water body or within 100 m of a water body, well or area frequented by people shall be reported immediately. Spills involving less than 10 liters of mixed pesticide or equivalent amount of unmixed formulation in areas not frequented by people, or remote from water bodies or wells shall be duly recorded by the Operations Supervisor. Records of all such incidents (spills) shall be kept on file by the Operator. Reporting of spill incidents shall be made to the Pesticides Control Section, Newfoundland Department of Environment, St. John's (ph. 729-3395) and to Environment Canada, St. John's (ph 772-2083).

10. All vehicles carrying liquid pesticide formulations shall carry a quantity of approved absorbent materials sufficient to contain the amount of product on hand. The vehicle shall also carry clean-up equipment such as shovels, rooms, bags, etc.
11. All pesticide storage sites shall be in accordance with Section 13 of *The Pesticides Control Regulations*.
12. Pesticides shall be stored in their original container or in a substitute container approved by the manufacturer. Substitute containers shall be labelled appropriately.
13. Concentrated pesticides transported in a vehicle during spray operations shall be contained in a locked box, secure area or compartment which must be locked while unattended. Pesticides shall not be transported in the passenger compartment of any vehicle.
14. The operator shall provide and ensure that all personnel involved in the mixing, loading, and application of pesticides wear appropriate protective equipment in accordance with the pesticide manufacturer's product label and / or Material Safety Data Sheet.
15. All exterior spraying activities are permitted only when wind speeds are between 2 and 15 km/hr; air temperatures are below 25° C; the relative humidity is above 50 % and it is not raining nor is rain anticipated over the next 2-hour period. Exceptions to wind speed conditions may be granted on a case by case basis. Contact the Pesticides Control Section for details.
16. **For pesticide operations involving a total of 750 ha or more**, dyking, security, storage and communications plans shall be provided and approved by the Pesticides Control Section in advance of any spray program for all locations where any pesticide is to be mixed or loaded.

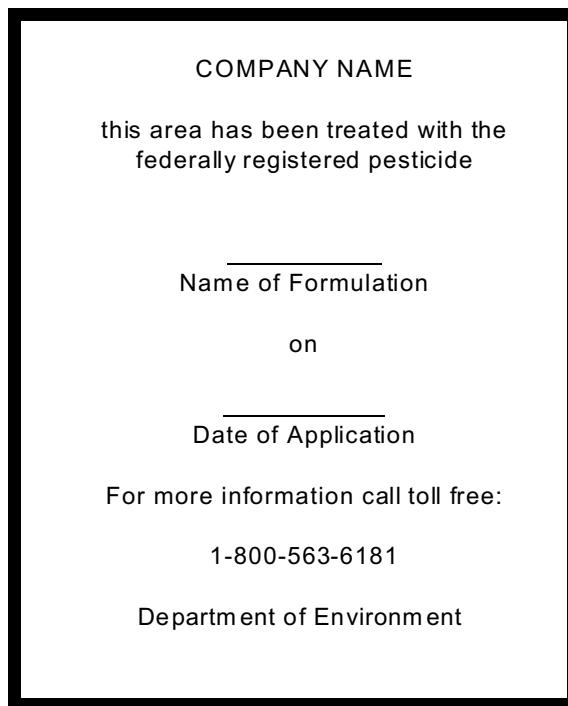
The operator will also be responsible for the development of contingency plans and associated call out notifications to the satisfaction of the Pesticides Control Section in advance of any spray program.

17. **For aerial insect control programs** (excluding agricultural, landscape - golf courses, or landscape - domestic lawn care), requests to treat proposed areas during the next seven calendar days period shall be submitted to the Pesticides Control Section (Mr. Roger Churchill, **ph.:** 709-729-6054; **Fax:** 709-729-6969) ; at least **one week** prior to said seven day period. At the end of the seven day period the Pesticides Control Section shall be notified of any future anticipated work in the manner described above.
18. Aerial spraying of pesticides is generally not permitted within Protected Water Supply Areas. The storage, mixing, loading and application of any pesticide within Protected Water Supply Areas requires a separate approval from the Water Resources Management Division of the Department of Environment. The approval request shall provide detailed information on the type and duration of activity, location of activity (to be delineated on 1:50 000 NTS topographical map), name of the pesticide along with its composition and toxicity data, application rate, application method, as well as any other information required.

The requirement of obtaining a separate approval from the Water Resources Management Division may be waived provided the above-noted information is provided to the Pesticides Control Section at the time of the submission of the pesticide operator licence application. The Water Resources Management Division will consult appropriate town council(s) before issuing any approval or consent for a pesticide operator license.

The operator assumes liability to provide an alternate source of water to the affected community or communities as a result of the source of water supply being contaminated due to the spray program.

19. For pesticide operations involving treatments of **pesticides applied aerially**, the public shall be advised of the purpose and scope of the project and of the issuance of this licence by means of a notice published in at least one (1) newspaper with circulation in municipalities whose boundaries encompass treatment areas. The newspaper ad will appear in any issue at least one week prior to commencing the program. The ad will state the area that is proposed for treatment over the next 21 calendar days, at the end of which time another ad is to be placed until the program is completed. The ad will contain the telephone numbers of the Pesticides Control Section, 709-729-3395, and 1-800-563-6181.
20. **For aerial insect control programs**, municipal governments whose boundaries encompass treatment and storage areas shall be notified prior to commencement of the programs. As per provisions of the Urban and Rural Planning Act and the Municipalities Act, any activity within a town boundary requires approval of the town council in question.
21. **For aerial insect control programs**, the public shall be advised of local treatments by the posting of signs in the area. The signs shall be as follows:



The particulars (location, timing, size of sign, etc.) of said posting shall be set by the Pesticides Control Section prior to spray programs.

22. The operator and/or his agent shall make every reasonable attempt to verbally notify adjacent owners, prior to the spray program, who, given the nature of the control operation, might be expected to benefit from said notification. In the event that this cannot be done, the operator shall use written notification to all dwellings to the satisfaction of the Pesticides Control Section.
23. For all programs involving the **aerial application of insecticides**, the operator shall be required to submit the details of public/municipality information programs to the Department of Environment. The details of said public/municipality information programs must be approved in advance by the Department of Environment. The operator may be required to carry out these programs following review by the Department of Environment.
24. In the event that formulations containing B.t.k. are to be used, the brochure **Protecting the**

Forests with Btk, is to be distributed to all municipal councils with boundaries that may contain spray blocks. In addition, the brochure is to be made readily available to members of the general public. Additional distribution is encouraged but is done so at the pesticide operator's discretion.

25. A toll-free information line shall be set up one week prior to commencement of the spray program, for the duration of the spray program, and will remain operational until September 30, 2001. The toll-free number will be advertised prior to the beginning of the spray program.
26. Daily notification through press releases shall be made by the licensed pesticide operator, for the duration of the spray program. Regular updates will be made regarding the status of the program. All updates will identify the toll-free information number.
27. For any pesticide application involving, either directly or indirectly, an aircraft of any sort, the operator shall maintain a **800 m buffer zone around all occupied osprey and bald eagle nests** during the period May 1 to August 15.
28. **Bacillus thuringiensis (B.t.k.) (PCP #24976)**
If approved for aerial application in Protected Public Water Supply Areas, the proponent shall provide the following widths of buffer zones, or any other buffer widths as specified by the Water Resources Management Division, along and around water bodies from the high water mark in a designated area:

<u>WATERBODY</u>	<u>WIDTH OF BUFFER ZONE</u>
Intake pond or lake	a minimum of 150 meters
River intake	a minimum of 150 meters for a distance of one (1) km upstream and 100 meters downstream
Main river channel	a minimum of 75 meters
Major tributaries, lakes or ponds	a minimum of 50 meters
Other waterbodies	a minimum of 30 meters

29. **Neemix 4.5 (azadirachtin) Temporary Registration # 26548**
For all aerial applications of Neemix 4.5, the operator shall maintain a minimum buffer of 100 meters from all recognized salmon rivers. The proponent will also maintain a minimum buffer of 50 meters from any body of water identified on a 1:50,000 NFS topographical map, any occupied cabin or other inhabited areas.
30. **Mimic 240 LV (tebufenozide) PCP Act #24502.**
For all aerial applications of Mimic 240LV, the operator shall maintain a minimum buffer of 100 meters from all recognized salmon rivers. The proponent will also maintain a minimum buffer of 50 meters from any body of water identified on a 1:50,000 NFS topographical map, any occupied cabin or other inhabited areas.
31. All pesticide mixing and rinsing sites shall be located a minimum of 100 m from the nearest water body. Loading of equipment with **water only** prior to the addition of pesticide can be done up to 5 m from a water body. Addition of pesticide to the water in the equipment shall be performed at least 100 m from the nearest water body.
32. Where water must be pumped directly into the formulation tank, an antiflow device must be fitted onto the pump and the siting should be that the formulating unit be at least 30 m from the watercourse and that the chemical not be opened for addition to the formulation tank until the equipment has been

filled with water and is out of the respective buffer zone.

33. **REVOCATION.**

Failure by an operator, its agent, employee or a licensed pesticide applicator under its control, to adhere to the Pesticides Control Act RSN 1990, c. P-8, the Pesticides Control Regulations, 1166/96, or the stipulations attached to its operator licence shall authorize the Minister of Environment to suspend, revoke, or cancel the subject licence or prosecute under section 25 of the Pesticides Control Act RSN 1990, c. P-8.

34. **PENALTY.**

Failure by an operator, its agent, employee or a licenced pesticide applicator under its control to comply with any of the terms and conditions of its licence is guilty of an offence under the Pesticides Control Act RSN 1990, c. P-8.

APPENDIX C



Regulatory Note

REG2000-13

Neemix 4.5[®]

The naturally occurring botanical insecticide Neemix 4.5[®], which contains the active ingredient azadirachtin for the control of sawflies in forestry in Canada, has been granted Section 17 temporary registration.

This regulatory note provides a summary of data reviewed and the rationale for the regulatory decision concerning this product.

(publié aussi en français)

October 16, 2000

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**Publications Coordinator
Pest Management Regulatory Agency
Health Canada
2250 Riverside Drive
A.L. 6606D1
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K1A 0K9**

**Internet: pmra_publications@hc-sc.gc.ca
www.hc-sc.gc.ca/pmra-arl/
Information Service:
1-800-267-6315 or (613) 736-3799
Facsimile: (613) 736-3798**

Foreword

Health Canada's Pest Management Regulatory Agency (PMRA) has issued a temporary registration for Neemix 4.5®, a naturally occurring botanical insecticide developed by Thermotrilogy Corporation. Neemix 4.5® contains the active ingredient azadirachtin, which is effective against sawflies in forestry.

Thermotrilogy Corporation will be carrying out additional chemistry, toxicological, and efficacy studies as a condition of this temporary registration. Following the review of this new data, the PMRA will publish a proposed registration decision document and request comments from interested parties before proceeding with a final regulatory decision.

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1.0 The active substances, its properties, uses, proposed classification, and labelling

1.1 Identity of the active substance and preparation containing it

Active substance: Azadirachtin

Function: Insecticide

Chemical name (IUPAC): No IUPAC name has been assigned

Chemical name (CAS): dimethyl [2aR-[2a'',3\$,4\$(1aR*,2S*,3aS*,6aS*,7S*,7aS*),
4a\$,5'',7aS*,=8\$(E),10\$,10a'',10b\$]]-10-(acetoxy)
octahydro-3,5-dihydroxy-4-methyl-8-[(2-methyl-1- oxo-2-
butenyl)oxy]-4-[(3a,6a,7,7a)-tetrahydro-6a-hydroxy-
7a-methyl-2,7-methanofuro[2,3-b]oxireno[e]oxepin-
1a(2H)-yl]-1H,7H=naphthal[1,8-bc:4,4a-c]difuran-5,
10a(8H)-dicarboxylate

CAS number: Azadirachtin A 11141-17-6
Azadirachtin B 95507-01-0

Nominal purity of active: 15%

Identity of relevant impurities of toxicological, environmental, or other significance:

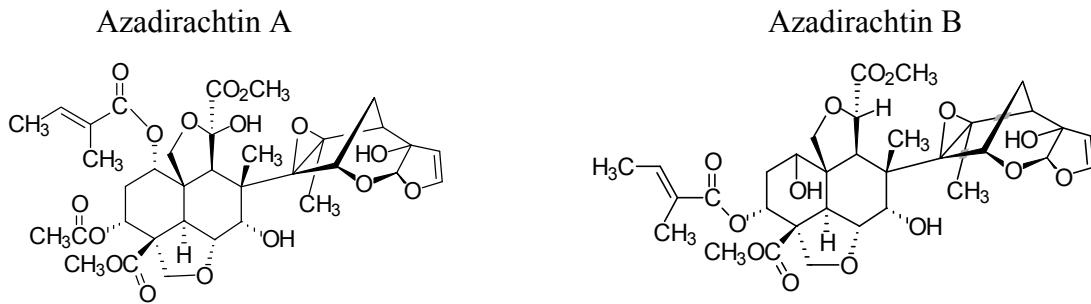
A small amount of aflatoxins may be present in the neem seeds that are the starting material in the manufacture of azadirachtin. The company has established standard operating procedures to minimize the amount of aflatoxins present in its source seeds. Implementing these procedures will insure that the aflatoxin level in the technical product will be a maximum of 80 ppb. Each lot of a technical material will be analysed for the aflatoxin level to insure that it is 80 ppb or less.

Toxic Substances Management Policy (TSMP) Track 1 substances as identified in Appendix II of Regulatory Directive DIR99-03 *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy* are not expected to be present in the product.

Molecular formula: C₃₅ H₄₄ O₁₆ (for Azadirachtin A)
C₃₃ H₄₂ O₁₄ (for Azadirachtin B)

Molecular mass: 720.7 (for Azadirachtin A)
662.7 (for Azadirachtin B)

Structural formula:



1.2 Physical and chemical properties of active substance

Technical product: Azadirachtin

Property	Result
Colour and physical state	Light mustard yellow amorphous solid
Odour	Sulfur
Melting point or range	85–105EC
Boiling point or range	Not applicable
Density	1.2 g/mL at 24EC
Vapour pressure	2.14 mm Hg at 20EC
UV and visible spectrum at 26EC	$\lambda_{\text{max}} = 220 \text{ nm}$
Water solubility (mg/mL)	2.8×10^{-5} at 10EC 5.0×10^{-5} at 25EC 3.0×10^{-4} at 50EC
Solubility in organic solvents	
acetone	2.0 mg/mL at 10EC
	6.25 mg/mL at 25EC
	9.5 mg/mL at 50EC
ethanol	0.05 mg/mL at 10EC
	0.125 mg/mL at 25EC
	3.75 mg/mL at 50EC
methanol	0.01 mg/mL at 10EC
	0.10 mg/mL at 25EC
	4.25 mg/mL at 50EC
hexane	<200 ppm at 25EC
<i>n</i> -Octanol–water partition coefficient (K_{ow})	12.3 ± 0.2

Property	Result
$\log K_{ow}$	1.09
Dissociation constant	Not applicable, no dissociable moieties
Stability (temperature, metals)	Expected to be stable under conditions of normal use

End-use product: Neemix 4.5®

Property	Result
Colour	Dark reddish brown
Odour	Banana-mint
Physical state	Liquid
Formulation type	Emulsifiable concentrate
Guarantee	4.5%
Container material and description	Plastic 0.5, 1.0, 5.0, and 10.0 L
Density	0.91 g/mL
pH	5.2
Storage stability	Stable when stored for 12 months at room temperature in commercial packaging
Surfactants	Atlox AL-1447

1.3 Details of uses

Neemix 4.5® is intended to be used by air against three sawfly species that are currently causing large scale damage to Canadian forests. It is recommended for control of the balsam fir sawfly (BFS) *Neodiprion abietis* (Harr.), the yellow-headed spruce sawfly (YHSS) *Pikonema alaskensis*, and the pine false webworm (PFW) *Acantholyda erythrocephala* by applying one application of between 20 and 50 g a.i./ha on early instars of larvae.

Balsam fir sawfly is a native species with wide distribution in Canada and the United States. BFS is an increasing problem in balsam fir stands in eastern Canada, most notably in western Newfoundland (for the year 2000, moderate to severe populations are expected in 40 000 ha of forest) and the Cape Breton and Eastern Shore regions of Nova Scotia. Its preferred host is balsam fir, but it may also feed on spruce. The larval stage of BFS feeds on foliage one-year-old and older. One year of feeding damage can cause extensive growth reduction for several years afterwards, making the weakened trees more

susceptible to attack by other organisms. Successive years of defoliation can lead to tree mortality.

Yellow-headed spruce sawfly is a serious pest of plantation and open grown spruce in many regions of North America. In Canada, the problem is particularly pronounced in the Bay of Fundy area and is also a concern in Quebec and Ontario. The young larvae feed only on the new or current year's foliage, but when almost full-grown they will feed on older needles. Persistent infestations will hinder growth development and greatly affect tree appearance, especially of young trees. Trees may even be killed outright after two years or more of severe defoliation, especially when the sawfly outbreak coincides with drought periods.

Pine false webworm is a web-spinning sawfly native to northern Europe and feeds on pines. Initially an occasional pest of young red pine plantations in Ontario, it is now attacking high value, semi-mature and mature red pine plantations, and tree mortality is occurring. It also has become a significant pest of large white pine in Ontario and New York. In Ontario, it is now threatening \$40 million worth of red pine plantations.

1.4 Classification and labelling

1.4.1 Azatin 15% Technical

The technical active Azatin 15% Technical is of low acute toxicity via oral, dermal and inhalation routes of exposure, non-irritating to the skin, minimally irritating to the eyes, and not a dermal sensitizer. None of the formulants in Azatin 15% Technical are on the Environmental Protection Agency (EPA) list of Inerts of Toxicological Concern (list 1) or List of Inerts for Priority Testing (list 2).

1.4.2 Neemix 4.5® end-use product

The formulation Neemix 4.5® is of low acute toxicity via oral, dermal, and inhalation routes of exposure, is moderately irritating to eyes, is minimally irritating to skin, and is not a dermal sensitizer. None of the formulants in Neemix 4.5® are on the Environmental Protection Agency (EPA) list of Inerts of Toxicological Concern (list 1) or List of Inerts for Priority Testing (list 2).

2.0 Methods of analysis

2.1 Methods for analysis of the active substance as manufactured

The high-performance liquid chromatography (HPLC) method with UV detection was used for the analysis of the active ingredient and the impurities. The linear range of the detector was sufficiently wide, and the method precision and accuracy were acceptable. The method provided was assessed and fully validated for the active ingredient.

The method linearity and specificity for the impurities was also confirmed. The information on precision and accuracy for the impurities was not provided. However, because of the biological and complex nature of the impurities, the requirement for accuracy and precision of the method has been waived.

2.2 Method for formulation analysis

An HPLC method with UV detection was used for the determination of the active ingredient in this product. The method has satisfactory specificity, linearity, precision, and accuracy and is suitable for use as an enforcement method.

3.0 Impact on human and animal health

3.1 Integrated toxicological summary

Azadirachtin (insect growth regulator) is the active compound in the technical active ingredients Neem Concentrate TGAI and Azatin 15% Technical, both of which contain a neem seed extract from the neem tree *Azadirachta indica* that grows in sections of India, Africa, Indonesia, and South America. Two data packages were submitted by the same registrant to support different uses. Because of deficiencies in both packages and the fact that the source of the two technical actives was the same (the hydrophilic moiety), the PMRA combined the available data from both packages for a more comprehensive review that allowed the establishment of no observed adverse effect levels (NOAELs) and conclusions regarding the potential for adverse health effects.

Neem Concentrate TGAI is of low acute toxicity via the oral and dermal routes of exposure, slightly toxic via the inhalation route of exposure, mildly irritating to eyes, slightly irritating to skin, and not a dermal sensitizer.

Azatin 15% Technical is of low acute toxicity via the oral, dermal, and inhalation routes of exposure, minimally irritating to eyes, non-irritating to skin, and not a dermal sensitizer. The formulation Neemix 4.5[®] is considered to be of low acute toxicity by the oral, dermal, and inhalation routes of exposure, moderately irritating to eyes, mildly irritating to skin, and not a dermal sensitizer.

Two short-term studies conducted in rats illustrated effects on haematological parameters (decreased mean corpuscular volume(MCV) and mean corpuscular haemoglobin (MCH), suggesting a slight hypochromic and microcytic anemia) at levels greater than 632 mg/kg bw/d. Leukocyte, lymphocyte, monocyte, and reticulocyte numbers were affected at the limit dose of 1000 mg/kg bw/d. The principal target organ was the liver, with increased liver weights and altered clinical chemistry parameters. At the limit dose of 1000 mg/kg bw/d, bile duct proliferation was also observed. The compound also caused effects on kidney, heart, adrenal gland, and ovary weights; however, no histopathological correlates were found for these organs. Gender sensitivity was not clearly evident in rats: the male was more sensitive showing more severe proliferation of

the bile ducts in the portal areas of the liver, whereas females demonstrated increased liver weights and increased gamma glutamyl transpeptidase levels at a lower dose level. The latter incidence may indicate possible hepatobiliary lesions. In the absence of chronic toxicity and carcinogenicity studies, the potential for the compound to cause toxicity following long-term exposure cannot be ruled out.

Although a decrease in adrenal and (or) ovary weights was noted in rats following 90-day dietary exposure, no histopathological correlates were found. However, based on the endocrine mode of action in insects and the absence of a reproductive toxicity study, the potential for the compound to cause endocrine effects cannot be ruled out. No neurological signs of toxicity were observed following dietary or gavage exposure at the limit dose of 1000 mg/kg bw/d.

Neem Concentrate TGAI was not mutagenic in bacterial and mammalian species in vitro and was found to be negative for inducing structural chromosomal aberrations in mice in vivo. Azatin 15% Technical was also not mutagenic in bacterial species. A developmental toxicity study with Neem Concentrate TGAI in rats demonstrated no toxic effects on the dams and no evidence was found of embryo or fetal toxicity or teratogenicity up to the limit dose of 1000 mg/kg bw/d.

Immunotoxicity was demonstrated in a study of Neem Concentrate TGAI treatment via oral gavage in female mice. In this study, body weight decreased by \$30% and food consumption was significantly reduced. Severe stress and malnutrition were related to an indirect immunomodulating effect. Although the dose selection may not be appropriate, the observed effects on spleen weight combined with the effects on plaque-forming cell (PFC) assay and the natural killer (NK) cell function confirm that Neem Concentrate TGAI can affect immune responses and that the effects may have clinical significance. None of these effects were observed when mice were dosed with Azatin 15% Technical via the dietary route, up to the highest dose of 1100 mg/kg bw/d. However, Azatin 15% Technical via dietary exposure caused suppression of cytotoxic T-lymphocyte function. In this study, the viability of the splenocytes was not reported, so it is possible that the results seen in the cytotoxic T-lymphocyte function test are associated with decreased viability of splenocytes and are not related to dosing.

Although limited, both data sets indicate potential immunotoxicity effects. Adequate immunotoxicity testing (Tier I) should be performed for Azatin 15% Technical and Neem Concentrate TGAI to support both the forestry use and any uses with potential for subchronic and chronic exposure. The results of Tier I testing will determine a need for Tier II immunotoxicity data.

For the short-term occupational exposure proposed for this forestry application, the lowest observed adverse effect level (LOAEL) based on effects on cytotoxic T-lymphocytes (500 ppm; 112 mg Azatin 15% Technical/kg bw/d) will be used. Other safety factors will be added to full personal protective equipment for workers to ensure that worker exposure is minimized. A full toxicology data package is required before any

expansion of forestry use or other uses involving subchronic and chronic exposure is considered for this product. This is based on the following:

- (i) evidence suggesting potential immunosuppression and lack of chronic data in two species to rule out the effect of immunosuppression on tumour formation;
- (ii) concern for potential adverse effects on endocrine system; compound has an endocrine mode of action in insects; 90-day rat dietary study demonstrated increases in adrenal and (or) ovary weights; no reproduction study available; and
- (iii) literature references indicating that neem oil (hydrophobic fraction of neem seed extract) has been associated with adverse reproductive effects (spermicidal activity, implantation failure; neem oil use as topical contraceptive in humans).

3.2 Determination of acceptable daily intake

Not being established.

3.3 Acute reference dose

Not being established.

3.4 Toxicology end-point selection for occupational and bystander risk assessment

Azatin 15% Technical is of low acute toxicity via oral, dermal, and inhalation routes of exposure, minimally irritating to eyes, non-irritating to skin, and not a dermal sensitizer. The formulation Neemix 4.5® is considered to be of low acute toxicity by the oral, dermal, and inhalation routes of exposure, moderately irritating to eyes, mildly irritating to skin, and not a dermal sensitizer.

For the short-term exposure proposed for this forestry application, the 30-day dietary mouse immunotoxicity study using technical Azatin 15% Technical was considered the most relevant study for toxicity end-point selection. Observed immunotoxicity in this study was considered to be the most sensitive end point in the data package. The LOAEL in this study was 112 mg/kg bw/d based on effects on cytotoxic T-lymphocyte function. A no observed adverse effect level (NOAEL) was not established for this study. The following are the main points considered in this decision:

- The anticipated exposure for mixers, loaders, and pilots will be of intermediate duration (i.e., four to six weeks) and intermittent throughout this period (e.g., four hours a day, several days per week).

- The predominant route of exposure is dermal. Inhalation is a minor route of exposure. A comparison of toxicity following dosing by oral, dermal, and inhalation routes (acute toxicity studies) did not indicate any increased route-specific systemic toxicity. Therefore, in the absence of any short-term toxicity study on the dermal or inhalation route of exposure, a toxicology study by the dietary route is considered appropriate for occupational risk assessment.
- Azatin 15% Technical and Neemix 4.5[®] were of low acute toxicity via the oral route, and no significant systemic toxicity was observed at a limit dose of 5000 mg/kg bw. In a short-term (90-day) dietary toxicity study in rats, the NOAEL was 161.4 and 32.1 mg/kg bw/d for males and females, respectively, based on observed altered haematological and clinical chemistry parameters. Changes in organ weights were observed at the higher dose level of 632.4 and 161.4 mg/kg bw/d for males and females, respectively; however, no histopathological correlates were observed for these organs.
- Gender sensitivity was not clearly evident in rats: the males had a more severe proliferation of the bile ducts in the portal areas of the liver; the females had an increase in liver weight and gamma glutamyl transpeptidase levels at a lower dose level than the males.
- In rats the test compounds were not mutagenic or clastogenic *in vivo* and was not teratogenic. However, immunotoxicity studies indicate that neem extract may have immunotoxic potential. Based on the observed suppression of cytotoxic T-lymphocyte function, the LOAEL for immunotoxicity for Azatin 15% Technical is 112 mg/kg bw/d.
- Although a decrease in adrenal and (or) ovary weights was noted in rats following a 90-day dietary exposure, no histopathological correlates were found. However, based on its endocrine mode of action in insects and the absence of a reproductive toxicity study, the potential for this compound to cause endocrine effects cannot be ruled out. No neurological signs of toxicity were observed following dietary as well as gavage exposure at the limit dose.

An additional 10-fold safety factor beyond the standard 100-fold is recommended to take into account use of a LOAEL for potential immunotoxicity and use of a Tier I data package.

3.5 Impact on human and animal health arising from exposure to Neemix 4.5[®]

3.5.1 Operator exposure assessment

Neemix 4.5[®] is an emulsifiable concentrate containing 40.4 g azadirachtin/L or 273 g total neem solids (including azadirachtin)/L. It is proposed for commercial, restricted registration for forest and woodlands management. The product would be applied once from June to early August by aerial application at a rate of 52.8 g azadirachtin/ha or 357 g total neem solids/ha.

Since Neemix 4.5[®] is derived from neem seeds, it may be contaminated with aflatoxins up to a maximum concentration of 24 ppb.

Neemix 4.5[®] would initially be used in Newfoundland, Nova Scotia, New Brunswick, and Ontario. Although in Newfoundland the degree of infestation is approximately 40 000 ha, the area that would be treated would be 4000–5000 ha. Treatment would take place over four to six weeks. On average pilots can treat 400 ha/day. Assuming the maximum application rate is used, 142.8 kg of total neem solids would be handled by mixers, loaders, and pilots in one day.

Mixer, loader, and pilot (applicator) exposure was estimated using the Pesticide Handlers Exposure Database version 1.1 (PHED 1.1). PHED is a compilation of generic mixer, loader, and applicator passive dosimetry data with associated software that facilitates the generation of scenario-specific exposure estimates. The PHED estimates meet criteria for data quality, specificity, and quantity outlined under the North American Free Trade Agreement Technical Working Group on Pesticides. Exposure was predominately dermal, with inhalation accounting for a minor component of overall exposure. Exposure estimates were based on the assumption that dermal absorption is equivalent to oral absorption.

To estimate exposure for each use scenario, appropriate subsets of A and B grade data were created from the mixer, loader, and applicator database files of PHED. All data were normalized for each kilogram of active ingredient handled. Exposure estimates are presented on the basis of the best-fit measure of central tendency, i.e., summing the measure of central tendency for each body part that is most appropriate to the distribution of data for that body part. The exposure estimates were based on one layer of clothing and gloves in PHED, with the exception of no gloves during ground application. A protection factor of 90% for chemical-resistant coveralls to be worn during mixing and loading was incorporated into the estimates.

The following exposure estimates and margins of exposure were derived for mixers, loaders, and pilots:

	Exposure (mg/kg bw/d)^a	Margin of exposure based on LOAEL of 112 mg/kg bw/d^b
Mixer and loader	0.0728	1540
Pilot	0.0213	5260

NOTE: Estimates are based on mixers and loaders wearing chemical-resistant coveralls over one layer of clothing and gloves and pilots wearing one layer of clothing and no gloves.

^a Based on a 70-kg operator and typical North American use patterns of 400 ha/day for custom mixers, loaders, and pilots. Dermal absorption was assumed to be equivalent to oral absorption.

^b Based on mouse immunotoxicity study.

These margins of exposure are acceptable.

Potential exposure estimates to aflatoxins were also derived using PHED based on the assumption that aflatoxins have identical transfer, deposition, and penetration characteristics as the active ingredient. Aflatoxin exposure for mixers and loaders wearing the same personal protective equipment described above was 0.0056 ng/kg bw/d. This exposure is much lower than aflatoxin intake of 1–2 ng/kg bw/d in Canadian children 1–11 years old (the age group with the highest exposure potential) from the consumption of peanuts or peanut butter. This estimate is based on results from the Health Protection Branch monitoring of aflatoxin residues in nuts and nut products (1985–1987).

3.5.2 Bystanders

Bystander exposure is expected to be low, with the provincial regulatory authorities implementing procedures such as public service announcements that would further reduce exposure potential.

3.5.3 Workers

Re-entry activities are minimal in forestry and are usually mechanized. Therefore a re-entry interval is not necessary.

4.0 Residues

4.1 Residue summary

Not applicable as this product is not intended for use on food.

5.0 Fate and behaviour in the environment

5.1 Fate and behaviour in soil

5.1.1 Soil transformation

Azadirachtin hydrolyzes at environmentally relevant pH. It is photolytically unstable. Therefore, hydrolysis and phototransformation will be the principal routes of transformation in the environment. Aerobic biotransformation of azadirachtin in soil is also a route of transformation in the environment. No major transformation products were identified in the hydrolysis, phototransformation, and biotransformation of neem extract (Appendix II, Table 1).

Azadirachtin is non-persistent to slightly persistent in aerobic soil under laboratory conditions (DT_{50} 6–25 days). A terrestrial field dissipation study was not available for review.

Azadirachtin rapidly transforms in the presence of heat, moisture, air, and sunlight.

5.1.2 Mobility

A leaching study using a 60-cm column with sandy loam forest soil showed that azadirachtin was not strongly bound to the soil particles. In this study, 21% of the applied compound was found in the top 0–10 cm, 44% in the next 10–20 cm, 16% in the bottom 20–30 cm of the column, and 8% in the leachate.

5.2 Expected environmental concentration in soil

Assuming a soil bulk density of 1.5 g/cm³, uniform distribution of the compound throughout a soil depth of 15 cm, and an application rate of 50 g a.i./ha to bare soil, the expected environmental concentration (EEC) in soil (EEC_{soil}) of azadirachtin is 0.022 mg a.i./kg.

5.3 Fate and behaviour in water

5.3.1 Aquatic transformation

Azadirachtin hydrolyzes at environmentally relevant pH. The rate of azadirachtin hydrolysis increases with an increase in alkalinity and an increase in temperature (Appendix II, Table 2).

5.3.2 Expected environmental concentrations in water

For a forestry scenario, the Tier I EEC in water (EEC_{water}) of azadirachtin from direct overspray of a body of water (15 cm deep) at the maximum recommended application rate of 50 g a.i./ha is 0.033 mg a.i./L. As a risk was indicated by the Tier I assessment, a Tier II assessment was triggered that took into account 50% interception by the forest canopy. This rate of interception was established through interdepartmental consultation with Fisheries and Oceans, Environment Canada, Natural Resources Canada (Forestry Sector) and the PMRA in 1996.

5.4 Fate and behaviour in air

The volatility of pure azadirachtin is unknown. Neemix 4.5[®] has a vapour pressure of 2.85×10^2 Pa, indicating that the product is highly volatile.

6.0 Effects on nontarget species

6.1 Effects on terrestrial nontarget species

6.1.1 Terrestrial organisms

Azadirachtin is practically nontoxic to the bobwhite quail on an acute and dietary basis. It is also nontoxic to the mallard duck on a dietary basis. Azadirachtin is nontoxic to the rat on an acute and dietary basis. Azadirachtin is nontoxic to honeybees (Appendix II, Table 3).

6.1.2 Aquatic organisms

The $\log K_{ow}$ value (1.9 at 25EC) indicates that azadirachtin has a negligible potential for bioconcentration or bioaccumulation in organisms. Azadirachtin is very highly toxic to fish and highly toxic to *Daphnia magna* on an acute basis (Appendix II, Table 4).

6.2 Environmental risk assessment

Risk to terrestrial and aquatic organisms from the use of azadirachtin was assessed using the margin of safety values (toxicity end point and EEC). Azadirachtin will not pose a risk to wild birds or mammals with the proposed use because it will take 50–60 days to reach the acute and dietary no observed effect concentrations (NOECs) for birds and more than three days to reach the acute NOEC for mammals. (The 50% dissipation time (DT_{50}) of azadirachtin in forestry foliage, soil, and litter ranges from 24 to 48 hours). Bees will not be at risk because the acute contact LD_{50} is equivalent to an application rate of 2.8 kg a.i./ha (Appendix II, Table 5). The Tier I aquatic risk assessment indicated that fish and daphnids might be adversely affected (margin of safety <1) (Appendix II, Tables 5 and 6); however, a more refined assessment that assumed a 50% interception by the forest

canopy (as established through the interdepartmental consultation mentioned above) indicated low risk to these organisms.

6.3 Environmental risk mitigation

The buffer zone necessary to protect sensitive aquatic species was calculated using the Agdrift model, which assumes a fine droplet size distribution, 50% interception by the canopy, 15-m maximum boom height above the canopy, and 16 km/h maximum wind speed. The end point selected was the acute NOEC for rainbow trout, which was the most sensitive aquatic species in the data provided. Although the model indicated that no buffer zone would be required, the PMRA has introduced an additional safety factor by requiring a 50-m buffer zone around aquatic resources.

7.0 Value

7.1 Effectiveness

Insect	Scientific name	Proposed application technique	Proposed rate	Proposed product
Balsam fir sawfly	<i>Neodiprion abietis</i>	Air or ground	20–50 g a.i./ha	523–1307 mL/ha

Results were submitted from two efficacy trials conducted in Newfoundland that examined aerial and ground application of Neemix 4.5® at various rates to control BFS. In summary, in 1996, Neemix 4.5® was applied aerially on first and second instar larvae at a rate of 50 g a.i./ha and significantly reduced a BFS populations by 90% while providing some foliage protection (63% whole-tree defoliation verses an average of 82% whole-tree defoliation in untreated controls) in trees containing extremely high populations of BFS (precounts of 50 larvae per branch). A below rate application of 10 g a.i. of Neemix 4.5®, applied aerially on first and second instar larvae, did not provide much reduction in BFS populations, although defoliation was reduced. In 1999, a ground application of Neemix 4.5® applied on third and fourth instar larvae at a rate of 45 g a.i./ha provided little protection of foliage or reduction in populations, possibly because of high rainfall after spraying. Neemix 4.5® applied by ground on third and fourth instar larvae at a rate of 20 g a.i./ha reduced populations slightly compared with controls and induced molting effects in BFS larvae. Sprayed trees were not defoliated any further.

Submitted efficacy data support label claims to apply between 20 and 50 g a.i./ha. However, the data do not allow for a determination of whether the lower rates are as efficacious as the higher rate of 50 g a.i./ha and do not allow for an assessment or determination of the criteria as to when to apply the high versus the low rate. The product should be applied on early instars of BFS, as 1999 spray trials conducted on third and fourth instar larvae did not appear to work as well as 1996 trials on first and second

instars. Further efficacy data would be required to confirm when the lower rate should be used and if the higher rate is necessary.

Insect	Scientific name	Proposed application technique	Proposed rate	Proposed product
Yellow-headed spruce sawfly	<i>Pikonema alaskensis</i>	Air or ground	25–50 g a.i./ha	654–1307 mL/ha

Results were submitted from two efficacy trials that examined aerial and ground application of Neemix 4.5® at various rates to control YHSS. In summary, in 1997, Neemix 4.5®, when applied aerially at 25 g a.i./ha, reduced YHSS populations by 66% and reduced tree defoliation to 9.2% compared with a trichlorfon standard applied at 500 g a.i./ha, which reduced YHSS populations by 76% and reduced tree defoliation to 9.4% (tree defoliation in the untreated blocks was 32.6 and 39.5%). In 1999, single and double applications of Neemix 4.5® by ground at a rate of 25 g a.i./ha produced minimal reductions in YHSS populations and defoliation; however, feeding was reduced in the treatment blocks. The ground applications were made on older larvae (fourth instar) and may have been too late to have a significant impact on YHSS populations.

The data support the label claims of applying between 25 and 50 g a.i./ha and would seem to indicate that the low rate of 25 g a.i./ha is as efficacious as the higher rate of 50 g azadirachtin per hectare. Further efficacy data would be required to confirm when the lower rate should be used and if the higher rate is necessary. The product should be applied on early instars of YHSS, as the 1999 spray trials conducted on later instar larvae did not appear to work as well as the 1997 trials conducted on earlier instar larvae. Only one application of Neemix 4.5® was sprayed in all trials; it is not known whether an extra application would improve the efficacy of the product.

Insect	Scientific name	Proposed application technique	Proposed rate	Proposed product
Pine false webworm	<i>Acantholyda erythrocephala</i>	Air or ground	25–50 g a.i./ha	654–1307 mL/ha

Results were submitted from one efficacy trial conducted in Ontario that examined aerial application of Neemix 4.5® at rates of 25 and 50 g a.i./ha to control PFW. Trees sprayed with Neemix 4.5® at rates of 25 and 50 g a.i./ha had 70.4 and 67.1% dead larvae at 9 days after treatment compared with 19.9% dead larvae found in untreated controls. End-of-season whole-tree defoliation estimates of the red pines indicated defoliation of 7.6% in trees sprayed with 25 g a.i./ha, 2.7% in trees sprayed with 50 g a.i./ha, and 40% whole-tree defoliation in untreated controls. Frass collections also indicated reduced feeding, as indicated at three weeks after treatment; one week's collection of frass from 10 trees showed 1.03 g frass collected under trees treated at 50 g a.i./ha, 2.14 g frass collected under trees treated at 25 g a.i./ha, and 16.24 g of frass collected under untreated trees. The lower rate of 25 g a.i./ha appeared to provide adequate protection of red pine foliage.

However, the data indicate that populations of PFW in the block treated at 25 g a.i./ha were approximately 33% the size of the populations of PFW treated at the higher rate of treatment of 50 g a.i./ha. Although the two rates of treatment showed comparable whole-tree defoliation of red pine (less than 10%, compared with untreated controls of 40%), it is not known from the data if the lower rate would provide the same degree of protection in trees as the higher rate with larger populations of PFW.

7.2 Alternatives

For Forestry or Woodlands use, few Pest Control Products are registered for control of sawfly species. The organophosphate insecticide fenitrothion is registered for sawfly control; another organophosphate insecticide, trichlorfon, has been used for YHSS and was used for control of BFS in Newfoundland under an Emergency Registration in 1999. It should be noted that all organophosphate insecticides are currently under re-evaluation in Canada. No other biological or chemical control products are registered for use against sawfly species in Canadian forests.

8.0 Toxic substances management policy considerations

Neem extract is derived from a natural source. Neem extract does not meet the TSMP Track-1 criteria for persistence in soil, water, and sediment or for bioaccumulation. Further, TSMP Track-1 materials as identified in Appendix II of Regulatory Directive DIR99-03 *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy* are not expected to be formed or present in the product.

9.0 Overall conclusions and regulatory decision

9.1 Assessments

9.1.1 Health risk assessment

Neem Concentrate TGAI (containing 4.5% azadirachtin) poses a slight acute toxicity hazard by the inhalation route. No significant acute hazard is associated with the oral and dermal routes.

Azatin 15% Technical (15% azadirachtin) poses no significant acute hazard via oral, dermal, or inhalation routes. The end use product (Neemix 4.5[®]) is moderately irritating to eyes and is mildly irritating to skin.

The Tier I data package included acute, short-term teratology, mutagenicity, and immunotoxicity studies. In mammals, Neem Concentrate TGAI is not considered to be fetotoxic or teratogenic, and both Neem Concentrate TGAI and Azatin 15% Technical are not considered to be genotoxic. A short-term study conducted in rats did not illustrate any major physiological effects in the test animals at the limit dose of 1000 mg/kg bw/d. The principal target organ was the liver.

Immunotoxicity was demonstrated in an immunotoxicity study following Neem Concentrate TGAI treatment via oral gavage in female mice with effects on spleen weight in combination with effects on the PFC assay and NK function. Azatin 15% Technical via dietary exposure caused suppression of cytotoxic T-lymphocyte function with no effect on any of the other immunotoxicity test parameters. In this study, the viability of the splenocytes was not reported and it is possible that the results seen in the cytotoxic T-lymphocyte function test are associated with decreased viability of splenocytes and are not related to dosing. Further immunotoxicity testing (Tier I) should be performed for Azatin 15% Technical and Neem Concentrate TGAI for continued forestry use in subsequent years, as well as any expansion of use with potential for subchronic and chronic exposure. The results of Tier I testing will determine a need for Tier II immunotoxicity data.

An intermediate-term mouse immunotoxicity study was determined to be the most relevant for the occupational risk assessment for mixers, loaders, and pilots. The margins of exposure (1500- to >5000-fold) for this proposed forestry use of Neemix 4.5®, calculated on the basis of typical North American use patterns, are considered acceptable.

A full toxicology data package is required before any expansion of forestry use or other uses involving subchronic and chronic exposures are to be considered for this product.

9.1.2 Environmental risk assessment

Risk to terrestrial and aquatic organisms from the use of azadirachtin was assessed using the margin of safety approach (toxicity end point and EEC). Azadirachtin will not pose a risk to wild birds or mammals with the proposed use because it will take 50–60 days to reach the acute and dietary NOECs for birds and more than three days to reach the acute NOEC for mammals. (The DT₅₀ of azadirachtin in forestry foliage, soil, and litter ranges from 24 to 48 hours). Bees will not be at risk because the acute contact LD₅₀ is equivalent to an application rate of 2.8 kg a.i./ha. Fish and aquatic invertebrates are unlikely to be affected at the proposed application rate assuming a 50% interception by the forest canopy. A 50-metre buffer zone provides an additional margin of safety for aquatic organisms.

9.1.3 Value assessment

Adequate data were provided from the aerial efficacy trials for BFS, YHSS, and PFW to support temporary registration; however, it was not possible to determine a clear dose response of the sawfly larvae to determine lowest effective rates. Further efficacy trials would be required in order to determine optimum rates of application.

Efficacy data generated for ground applications were inadequate to allow for efficacy assessment (late instars, rainfall events) and further data are required.

The product should be applied on early instars of sawfly.

Based on the mode of action of azadirachtin and other neem by-products in the formulation, there may be other effects besides immediate population reductions. Nonlethal effects were noted by the study authors (e.g., effects on moulting, antifeedant effects); however, these effects were not quantified in the submitted studies.

9.2 Label amendments and recommendations

Primary display panel:

The label classification will be RESTRICTED only.

The signal words WARNING EYE IRRITANT should be added.

The statement KEEP OUT OF REACH OF CHILDREN should be moved to the secondary display panel under PRECAUTIONS.

Secondary display panel:

Replace the existing statement with
KEEP OUT OF REACH OF CHILDREN.

The following changes should be added to the PRECAUTIONS section of the label:

- When handling the concentrate, and during mixing, loading, clean-up, and repairs, the following personal protective equipment must be worn: chemical-resistant coveralls over long-sleeved shirt, long pants, chemical-resistant gloves, rubber boots, protective eyewear, and headgear.
- Pilots must wear a long-sleeved shirt, long pants, shoes, and socks.
- For aerial application to forests and woodlands only. (Any reference to ground application must be removed from the label.)

The following statements on the Neemix 4.5® label are required under Environmental Hazards:

- Do not apply at a boom height higher than 15 m above canopy.
- Aerial drift is increased under certain meteorological conditions. Do not apply during periods of dead calm, when winds are gusty, or when wind speed is greater than 16 km/h at the flying height.
- For the protection of nontarget habitats, overspray, or drift to sensitive habitats must be avoided. A buffer zone of 50 downwind edge of the boom and sensitive aquatic habitats such as sloughs, ponds, lakes, rivers, streams, and wetlands. Do not contaminate these habitats when cleaning and rinsing spray equipment or containers.

Directions for Use are to be enclosed in a solid black line box along with Restricted Uses and the following text added:

- NATURE OF THE RESTRICTION: This product is to be used only in the manner authorized. Contact local pesticide regulatory authorities about use permits that may be required.
- Application is to be by air only.

9.3 Regulatory decision

Azatin 15% Technical and Neemix 4.5® have been granted a temporary registration for aerial forestry use for sawflies, pursuant to Section 17 of the PCP Regulations, subject to the generation of the following studies and clarifications:

- a revised Control Product Specification Form listing the correct common names of the impurities;
- results of the analysis for the content of aflatoxins in each batch of Azatin 15% Technical produced;
- immunotoxicity testing of Neem Concentrate TGAI and Azatin 15% Technical: Tier I immunotoxicity testing using currently recommended methods, followed by Tier II immunotoxicity testing if triggers are observed in Tier I;
- efficacy data for ground application; and
- efficacy trials (aerial operational trials) conducted at the rate range proposed on the label.

List of abbreviations

a.i.	active ingredient
ADI	acceptable daily intake
BFS	balsam fir sawfly
CAS	Chemical Abstracts Service
DT ₅₀	dissipation time at 50%
EEC	expected environmental concentration
EPA	Environmental Protection Agency
IUPAC	International Union of Pure and Applied Chemistry
LC ₅₀	lethal concentration 50%
LD ₅₀	lethal dose 50%
LOAEL	lowest observed adverse effect level
MAS	maximum average score
MCH	mean corpuscular haemoglobin
MCV	mean corpuscular volume
MIS	maximum irritation score
NK	natural killer cell
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
PCP	Pest Control Products
PFB	pine false webworm
PFC	plaque-forming cell assay
PHED	Pesticide Handlers Exposure Database
ppb	parts per billion
ppm	parts per million
PMRA	Pest Management Regulatory Agency
<i>t</i> _½	half-life
TSMP	Toxic Substances Management Policy
YHSS	yellow-headed spruce sawfly

Appendix I Toxicology

Table 1 Neem Concentrate TGAI

Study type	Species and strain and dose	LD ₅₀ (mg/kg bw) and LC ₅₀ (mg/L)	Degree of toxicity and significant effects
Acute toxicity			
Oral	Rat (Sprague-Dawley), 5/sex 5000 mg/kg bw purity: 4.5% a.i.	LD ₅₀ >5000 mg/kg bw	Low toxicity One animal lost hair, one animal had dark red mottled lungs.
Dermal	Rabbit (New Zealand White), 5/sex 2000 mg/kg bw purity: 4.5% a.i.	LD ₅₀ > 2000 mg/kg bw	Low toxicity Dermal irritation, soft stools, faecal stain, clear ocular discharge were observed.
Inhalation	Rat (Sprague-Dawley), 5 0.54 or 5.33 mg/L purity: 4.5% a.i.	LC ₅₀ = 0.54 – 5.33 mg/L	Slight toxicity Urine stain, breathing abnormalities, swollen eyelid(s), 9 activity, rough coat, unkempt appearance, hair loss.
Eye irritation	Rabbit (New Zealand White), 2 %, 4 & 0.1 mL undiluted purity: 4.5% a.i.	Maximum average score (MAS) = 8.89 (Maximum irritation score (MIS) = 11.17 at 24 h)	Mildly irritating Corneal opacity (1/6) and conjunctivitis (6/6), resolved by day 7–10.
Dermal irritation	Rabbit (New Zealand White), 2 %, 4 & 0.5 mL undiluted purity: 4.5% a.i.	MAS = 1.04	Slightly irritating Erythema and edema resolved by 72 h.
Dermal sensitization (Buehler test)	Guinea Pig (Dunkin-Hartley), 20 % purity: 4.5% a.i. 40% (1 st induction), 100% (2 nd and 3 rd inductions and challenge)	Negative	Not a dermal sensitizer

Study	Species and strain or cell type	Dose	Significant effects and comments
Genotoxicity			
Ames test	<i>S. typhimurium</i> ± S9 purity: 2.3% a.i.	100, 333, 667, 1000, 3330 or 5000 Fg/plate	Negative
Forward mutations at the thymidine kinase locus (in vitro)	Mouse lymphoma L5178Y cell line, ± S9 purity: 2.3% a.i.	12.5–150 Fg/mL	Negative
Structural chromosomal aberrations in vivo (micronucleus test)	Mice purity: 4.5% a.i.	1250, 2500 or 5000 mg/kg bw	Negative
Study	Species (strain) and dose	NOAEL and LOAEL (mg/kg bw/d)	Significant effects at different doses (mg/kg bw/d) and comments
Subchronic toxicity			
Dietary (90 days)	Rat (Sprague-Dawley Control: CD®BR VAF Plus), 10/sex/group 0 or 1000 mg/kg bw/d purity: 4.5% a.i.	LOAEL: 1000 NOAEL: Not determined	1000: \ body wt & body wt gain (%,&); \ MCV & MCH (%); \ leukocytes (&), \ lymphocytes (&), \ monocytes (&), [reticulocytes (&), \ glucose (%,&), [cholesterol (&), [creatinine (%,&), \ triglycerides (%,&), [alkaline phosphatase (%,&), \ organ wts (kidney, heart & adrenal in %,& and ovary in & with no histopathology observed); [liver wts (%,&), bile duct proliferation (%,&)
Reproductive and developmental toxicity			
Teratogenicity	Rat (Sprague-Dawley), 25/group 10, 100 or 1000 mg/kg bw/d by gavage on gestation days 6–15 purity: 4.5% a.i.	Maternal: NOAEL = 1000 Embryo or fetal: NOAEL = 1000	No toxicity was observed up to the dose level of 1000 mg/kg bw/d (high dose). Not teratogenic
Special studies (immunotoxicity)			
Gavage (30 d)	Mice (B ₆ C ₃ F ₁), 40 &/dose 0, 250, 500, or 1000 mg/kg bw/d purity: 4.5% a.i. Positive controls: Cyclophosphamide (80 mg/kg bw), <i>N</i> -deacetyl- <i>N</i> -methylcolchicine (0.1 Fg/mL) and recombinant human interleukin-2 (optimal concentration)	LOAEL: 250 NOAEL: Not determined	\$250: \ body wt gain, \ food consumption, [water intake, \ spleen wt, \ IgM antibody forming cells in response to sheep red blood cells, \ basal NK cell activity 1000: [platelet counts, \ augmented (IL-2) NK-cell function.

Table 2 Azatin 15% Technical and Neemix 4.5®

Study type	Species, strain, and dose	LD ₅₀ (mg/kg bw) and LC ₅₀ (mg/L)	Degree of toxicity and significant effects
Acute toxicity for Azatin 15% Technical			
Oral	Rat (Sprague-Dawley) 5/sex 5000 mg/kg bw purity: not stated	LD ₅₀ > 5000 mg/kg bw	Low toxicity Lethargy, hunched posture.
Dermal	Rabbit (New Zealand White); 5/sex 2000 mg/kg bw purity: not stated	LD ₅₀ > 2000 mg/kg bw	Low toxicity Dermal irritation, transient diarrhea.
Inhalation	Rat (Sprague-Dawley) 2.41 mg/L (4 h) purity: not stated	LC ₅₀ > 2.41 mg/L	Low toxicity Clear nasal discharge, salivation, redness around the eyes and rales, mouth breathing, wheezing.
Eye irritation	Rabbit (New Zealand White), 3/sex 0.1 g undiluted purity: 8.65% a.i.	MAS = 2.2	Minimally irritating No corneal opacity, iritis (2/6) at 1-h only, erythema and chemosis (6/6), resolved by day 2–3.
Dermal irritation	Rabbit (New Zealand White), 3/sex 0.5 g undiluted purity: 8.6% a.i.	MAS = 0	Non-irritating
Dermal sensitization (Buehler test)	Guinea pig (Hartley), 10 %/group purity: 19.2% a.i. 25% (induction), 0.5% (challenge)	Negative	Not a dermal sensitizer
Acute toxicity for Neemix 4.5®			
Oral	Rat (Sprague-Dawley), 5/sex 5000 mg/kg bw	LD ₅₀ > 5000 mg/kg bw	Low toxicity Transient incidences of rales, urine stains, rough coat, dark material around the fecal area.
Dermal	Rabbit (New Zealand White), 5/sex 2000 mg/kg bw	LD ₅₀ > 2000 mg/kg bw	Low toxicity Transient incidences of faecal stain and dark material around the fecal area.
Inhalation	Rat (Sprague-Dawley), 5/sex 2.05 mg/L (4 h)	LC ₅₀ > 2.05 mg/L	Low toxicity Breathing abnormalities, 9 defecation, wobbly gait, 9 activity, piloerection, lacrimation, urine stain and dark material around the fecal area.
Eye irritation	Rabbit (New Zealand White), 6 & 0.1 mL undiluted	MAS = 23.89 (MIS = 39 @ 1h in 1 animal)	Moderately irritating Corneal opacity (4/6) at 24 h, resolved by day 10.

Study type	Species, strain, and dose	LD ₅₀ (mg/kg bw) and LC ₅₀ (mg/L)	Degree of toxicity and significant effects
Dermal irritation	Rabbit (New Zealand White), 1 % and 5 & 0.5 mL undiluted	MAS = 1.71	Mildly irritating Very slight to slight erythema (6/6), resolved by day 7.
Dermal sensitization (Buehler test)	Guinea pig (Hartley albino), 5/sex/group 25, 50, 75, or 100% (induction & challenge)	Negative	Not a dermal sensitizer
Study	Species or strain or cell type	Doses employed	Significant effects and comments
Genotoxicity			
Ames test	<i>S. typhimurium</i> ± S9 (purity: 8.6% a.i.)	5, 1, 0.5, 0.05, or 0.005 mg/plate	Negative
Study	Species or strain and doses	NOAEL or LOAEL (mg/kg bw/d)	Significant effects at different doses (mg/kg bw/d) and comments
Subchronic toxicity			
Dietary (90 d)	Rat (Sprague-Dawley Crl:CD®BR VAF Plus), 10/sex/group 0, 500, 2500 or 10 000 ppm (0, 32.1, 161.4 or 632.4 mg/kg bw/d) purity: 7.74 % a.i.	LOAEL: 632 (%) 161 (& NOAEL: 161 (%) 32 (&)	161.4: [gamma glutamyl transpeptidase (&), [liver wt (& 632: \ body wt, body wt gain & food consumption (%,&); \ MCV, MCH & MCHC (%); \ haemoglobin, hematocrit & MCV (&); [blood urea nitrogen (%), [gamma glutamyl transpeptidase (%,&), [creatinine (&), [liver wt (%,&) and \ ovary wt (&) with no histopathology observed
Special studies (immunotoxicity)			
Dietary (30 d)	Mice (B ₆ C ₃ F ₁), 40 &/dose 0, 500, 1250 or 5000 ppm (0, 112, 295 or 1100 mg/kg bw/d) purity: 7.74% a.i. Positive controls: Cyclophosphamide (80 mg/kg bw), <i>N</i> -deacetyl- <i>N</i> -methylcolchicine (0.1 Fg/mL) and recombinant human interleukin-2 (optimal concentration)	Immunotoxicity LOAEL: 112 NOAEL: Not determined	\$112: \ cytotoxic T-lymphocyte function 1100: \ body weight gain possibly due to palatability, [platelet counts

Appendix II Environmental Assessment

Table 1 Summary of terrestrial fate and transformation data

Process	End point	Comments
Hydrolysis	$t_{1/2}$ at 20EC pH 4 19 d pH 7 13 d pH 10 2 h	Buffered solutions. Hydrolysis is greatly influenced by pH in the order pH 10>>pH7>pH4. Hydrolysis is a principal route of transformation at neutral and basic pH.
	$t_{1/2}$ at 20EC pH 8±0.5 7 d	Pond water. Hydrolysis is a route of transformation at neutral pH.
	$t_{1/2}$ at 35EC pH 5 11.5 d pH 7 2.4 d pH 8 0.5 d	Buffered solutions. Hydrolysis is a principal route of transformation at neutral and basic pH. At 25EC and pH 7, $t_{1/2}$ was 11 d; hydrolysis of azadirachtin is greatly influenced by temperature.
	$t_{1/2}$ at 35EC pH 6.2 21 d pH 7.3 2 d pH 8 0.5 d	Natural waters. Hydrolysis is a principal route of transformation at neutral and basic pH.
Phototransformation	$t_{1/2}$ 7 d	Study conducted on plant. Phototransformation is a principal route of transformation.
Aerobic biotransformation	DT ₅₀ 26 d at 22EC	Greenhouse study on nursery soil. Aerobic biotransformation will be a route of transformation.
	DT ₅₀ 6 d	Study conducted with Margosan O (0.25% azadirachtin). The study is a combination of biotransformation and leaching. As such, the methodology did not conform with guidance offered in T-1-255, Guidelines for Determining Environmental Chemistry and Fate of Pesticides.
Anaerobic biotransformation	No data available.	
Adsorption or desorption	K _{oc} 5.1–7.9	Azadirachtin has high mobility in forestry sandy loam soil.
Soil column leaching	21% in 0–10 cm 44% in 10–20 cm 16% in 20–30 cm 8% in leachate	Azadirachtin has a potential for leaching in sandy loam soil.
EEC in soil	0.022 mg a.i./kg dry soil	

Table 2 Summary of aquatic fate and transformation data

Process	End point	Comments
Hydrolysis	$t_{1/2}$ at 20EC pH 4 19 d pH 7 13 d pH 10 2 h	Buffered solutions. Hydrolysis is greatly influenced by pH in the order pH 10 >> pH7 > pH4. Hydrolysis is a principal route of transformation at neutral and basic pH.
	$t_{1/2}$ at 20EC pH 8±0.5 7 d	Pond water. Hydrolysis is a route of transformation at neutral pH.
	$t_{1/2}$ at 35EC pH 5 11.5 d pH 7 2.4 d pH 8 0.5 d	Buffered solutions. Hydrolysis is a principal route of transformation at neutral and basic pH. At 25EC and pH 7 $t_{1/2}$ was 11d; hydrolysis of azadirachtin is greatly influenced by temperature.
	$t_{1/2}$ at 35EC pH 6.2 21 d pH 7.3 2 d pH 8 0.5 d	Natural waters. Hydrolysis is a principal route of transformation at neutral and basic pH.
Phototransformation	No data available.	
Aerobic biotransformation	No data available.	
Anaerobic biotransformation	No data available.	
EEC in water (Tier I, direct overspray)	0.033 mg a.i./L	Forestry use

Table 3 Summary of toxicity of azadirachtin for terrestrial organisms

Group	Organism	Study	NOEC	LD ₅₀ and LC ₅₀	Degree of toxicity
Birds	Bobwhite quail	acute oral	29.2 mg a.i./kg bw	LD ₅₀ > 225 mg a.i./kg bw	Moderate
	Bobwhite quail	acute oral	477 mg a.i./kg diet	LC ₅₀ > 477 mg a.i./kg diet	Moderate
	Bobwhite quail	dietary	1111 mg a.i./kg diet	LC ₅₀ > 1111 mg a.i./kg diet	Slight
	Bobwhite quail	dietary	316 mg a.i./kg diet	LC ₅₀ > 562 mg a.i./kg diet	Moderate
	Mallard duck	dietary	278 mg a.i./kg diet	LC ₅₀ > 1111 mg a.i./kg diet	Slight
Mammals	Rat	acute oral		LD ₅₀ > 5000 mg Azatin/kg bw	None
	Rat	acute oral		LD ₅₀ > 5000 mg Neemix/kg bw	None
	Rat	90 d dietary (7.74% a.i.)	LOAEL: 632 mg Azatin/kg bw/d (%) 161 mg Azatin/kg bw/d (& NOAEL: 161 mg Azatin/kg bw/d (%) 32 mg Azatin/kg bw/d (&)		
	Mouse	30 d (7.74% a.i.)	LOAEL: 112 mg Azatin/kg bw/d(&)		Potentially immunotoxic
Soil organisms	Earthworm	acute		0.0264 kg a.i./ha (field application) had no effect on population	
Predators and parasites	Honeybees	acute contact		LD ₅₀ > 2.5 Fg a.i./bee	Moderate

Table 4 Summary of toxicity of azadirachtin to aquatic organisms

Group	Organism	Study	NOEC (mg a.i./L)	LC ₅₀ (mg a.i./L)	Degree of toxicity
Fish	Rainbow trout	Acute	0.016	0.048	Very high
	Bluegill sunfish	Acute	0.06	0.11	High
Invertebrates	Water flea	Acute	0.13	1.0	High
	Water flea	Acute	0.03	0.039	Very high

Table 5 Summary of risks to terrestrial organisms

Organism	Effect	Toxicity end point	EEC	Margin of safety	Risk	Mitigative measures
Bobwhite quail	Acute oral	NOEC = 29.2 mg a.i./kg bw	6 mg a.i./kg dw	60 days	no risk	not required
Bobwhite quail	Dietary	NOEC = 316 mg a.i./kg diet	6 mg a.i./kg dw	52.7	no risk	not required
Mallard duck	Dietary	NOEC = 278 mg a.i./kg bw	1.7 mg a.i./kg dw	164	no risk	not required
Rat	Acute oral	LD ₅₀ > 5000 mg Neemix 4.5®/kg bw (i.e., >1111 mg a.i./kg bw)	25.2 mg a.i./kg dw	>3.3 days	no risk	not required
Earthworm	Acute	0.0264 kg a.i./ha (field application) had no effect on population	0.022 mg a.i./kg		no risk	not required
Honeybees	Acute contact	LD ₅₀ > 2.5 Fg a.i./bee or 2.8 kg a.i./ha*	50 g a.i./ha		no risk	not required

* Fg/bee is converted to g/ha by multiplying with 1.12.

Table 6 Summary of Tier I risk assessment to aquatic organisms

Organism	Effect	NOEC (mg a.i./L)	EEC (mg a.i./L)	Margin of safety	Risk
Water flea	Acute	0.03	0.033	0.9	Risk*
Rainbow trout	Acute	0.016	0.033	0.4	Risk*

* Tier II assessment is triggered.

2000.12.01

NEEMIX**7** 4.5

RESTRICTED

READ THE LABEL BEFORE USING

GUARANTEE: Azadirachtin 4.5%

WARNING EYE IRRITANT

This product contains 40.4 grams (0.34 pounds) of
azadirachtin per Liter (U.S. gallon)

REGISTRATION NO. 26548 PEST CONTROL PRODUCTS ACT

Net Contents: Liters

MANUFACTURED BY
THERMO TRILOGY(TM) CORPORATION
9145 GUILFORD ROAD, SUITE 175
COLUMBIA, MD 21046

NOTICE TO USER:

This control product is to be used only in accordance with the directions on this label. It is an offense under the Pest Control Products Act to use a control product under unsafe conditions.

NATURE OF RESTRICTION: This product is to be used only in the manner authorized; contact local pesticide regulatory authorities about use permits that may be required.

RESTRICTED USES:

Forest Management Use: Aerial Application for sites greater than 500 ha.

Woodlands Management Use: Aerial Application for sites 500 ha or less.

DIRECTIONS FOR USE

For use in conifer forests and woodlots on the following:

Insect	Scientific Name	Grams AI/Ha	Product/Ha
Balsam Fir Sawfly	<i>Neodiprion abietis</i>	20-50 g ai/ha	523 to 1307 mL/ha
Yellow-headed Spruce Sawfly	<i>Pikonema alaskensis</i>	25-50 g ai/ha	654 to 1307 mL/ha
Pine False Webworm	<i>Acantholyda erythrocephala</i>	25-50 g ai/ha	654 to 1307 mL/ha

Dilute Neemix 4.5 in sufficient amounts of water to obtain the desired application rate of 20-50 g ai/hectare.

Neemix 4.5 can only be applied using aerial application equipment. Application should be made against small larvae (early instars).

Before using this product, consult your local Canadian Forest Service office or forestry authority and Thermo Trilogy Corporation for information on timing, method of application, and concentration of spray mixtures.

PRECAUTIONS

KEEP OUT OF REACH OF CHILDREN

WARNING

Causes substantial but temporary eye injury. Do not get in eyes or on clothing. Wear goggles and/or face shield. Wash thoroughly with soap and water after handling. Remove contaminated clothing and wash clothing before reuse. Harmful if swallowed. Avoid contact with skin, eyes, or clothing. Avoid contamination of feed and foodstuffs. Avoid breathing spray mist. In case of eye contact, flush eyes with plenty of water. If on skin, wash with soap and water. If irritation persists, get medical attention.

When handling the concentrate, and during mixing, loading, clean-up and repairs, the following personal protective equipment must be worn: chemical-resistant coveralls over long-sleeved shirt, long pants, chemical-resistant gloves, rubber boots, protective eyewear and headgear.

Pilots must wear long-sleeved shirt, long pants, shoes and socks.

For aerial application to forests and woodlands only.

Do not use or store near heat or open flame.

Environmental Hazards

This product may be hazardous to fish and aquatic invertebrates. Do not apply directly to water, or to areas where surface water is present, or to intertidal areas below the mean high water mark.

Aerial drift is increased under certain meteorological conditions. Do not apply during periods of dead calm, when winds are gusty or when wind speed is greater than 16 km/hr at the flying height. Do not apply at the boom height higher than 15 m above canopy.

For the protection of non-target habitats, overspray or drift to sensitive habitats must be avoided. A buffer zone of 50 m is required between the downwind edge of the boom and sensitive aquatic habitats such as sloughs, ponds, lakes, rivers, streams, and wetlands. Do not contaminate these habitats when cleaning and rinsing spray equipment or containers.

FIRST AID

IF IN EYES: Hold eyelids open and flush with a steady, gentle stream of water for 15 minutes. Get medical attention.

IF ON SKIN: Wash with plenty of soap and water. Get medical attention if irritation persists.

IF INHALED: Remove victim to fresh air. If not breathing, give artificial respiration, preferably mouth-to-mouth. Get medical attention if irritation persists.

IF INGESTED: Contact a poison control centre or

physician, in case of ingestion.

Take container, label or product name and Pest Control Registration Number with you when seeking medical attention.

TOXICOLOGICAL INFORMATION

Treat symptomatically

DISPOSAL

1. Triple- or pressure-rinse the empty container. Add the rinsings to the spray mixture in the tank.
2. Follow provincial instruction for any required additional cleaning of the container prior to its disposal.
3. Make the empty, container unsuitable for further use.
4. Dispose of the container in accordance with provincial requirements.
5. For information on disposal of unused, unwanted product, contact the manufacturer or the provincial regulatory agency. Contact the manufacturer and the provincial regulatory agency in case of a spill, and for clean-up of spills.

NOTICE TO BUYER

Seller's guarantee shall be limited to the terms set out on the label and, subject thereto, the buyer assumes the risk to persons or property arising from the use or handling of this product and accepts the product on that condition.

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