

## AMITRAZ

The purpose of this Decision Document is to announce Agriculture and Agri-Food Canada's decision, in consultation with Health Canada and Environment Canada, to register Amitraz Technical (Registration No. 23485) and Mitac WP (Registration No. 23486) for control of pear psylla in commercial pear orchards. This document also provides background information on the benefits and human health and environmental risk assessments considered in arriving at this decision.

*(publié aussi en français)*

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**Since this document was prepared, responsibility and resources for pesticide regulation have been consolidated within the new Pest Management Regulatory Agency under Health Canada, effective April 1, 1995.**

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## Background

In January 1991, the Plant Industry Directorate published *Note to CAPCO C91-01* which summarized the status of the proposed use of amitraz for control of pear psylla in pear orchards. In summary, Mitac WP (a wettable powder formulation of amitraz) could not be registered for control of pear psylla because of the following human health and environmental concerns:

- ! Health Canada had concluded that residues of amitraz expected to occur on treated pears would incur an unacceptable risk of harm to certain sectors of the Canadian population eating treated pears. As a result, Health Canada was not prepared to establish a Maximum Residue Limit (MRL) for the proposed use of amitraz on pears as required under the *Food and Drugs Act* administered by Health Canada.
- ! Based on the available exposure information, Health Canada had concluded that there was no adequate margin of safety for farmers during mixing/loading and application of amitraz wettable powder. Also, the available data did not allow for an assessment of third-party exposure (e.g., people entering orchards after amitraz application) and subsequent risk.
- ! Additional information was required by Environment Canada to assess the fate of amitraz in the environment and the risk to wildlife.

Since publication of *Note to CAPCO C91-01*, the manufacturer of amitraz (AgrEvo Canada Inc., formerly NOR-AM Chemical Company of Wilmington, Delaware) amended the proposed use pattern for Mitac WP and developed new information to address the outstanding human health and environmental concerns.

Further review in light of these additional data has allowed Health Canada to propose an MRL of 1.0 ppm and support registration of amitraz for use on pears in Canada. Environment Canada advises that the recently submitted environmental data has reduced previous concerns regarding the exposure of birds and wild mammals to amitraz residues.

## Use Pattern

The use pattern for Mitac WP has been amended from that considered for registration in *Note to CAPCO C91-01*. AgrEvo Canada Inc. reduced the maximum number of applications of Mitac WP permitted per season and increased the period of time between the last application and harvest. The current use pattern for Mitac WP is as follows:

Mitac WP is registered for control of pear psylla in commercial pear orchards. The registered rate of application is 1.65 to 3.35 kg of Mitac WP per hectare (0.83 to 1.68 kg active ingredient per hectare). A maximum of two applications are permitted per season. Allow at least 14 days between applications. The last application should not be applied within 14 days of harvest. Application should be timed when pear psylla are in the adult or young nymphal stages of development. Mitac WP is registered for application by ground equipment only (i.e., aerial application is not permitted). A buffer zone of 100 metres from water should be observed when applying Mitac WP with an air-blast sprayer.

## International Considerations

Amitraz is registered in over 60 countries world-wide for insect and mite control on livestock and agricultural crops. MRLs have been adopted by the Codex Committee on Pesticide Residues for commodities such as cattle meat (0.05 ppm), cherries (0.5 ppm), cotton seed (0.5 ppm), cucumber (0.5 ppm), hog meat (0.05 ppm), oranges (0.5 ppm), peach (0.5 ppm), pome fruits (0.5 ppm), sheep meat (0.1 ppm) and tomatoes (0.5 ppm).

Amitraz is registered in the United States for mite control on livestock, mite and pear psylla control on pears, and mite and insect control on cotton. The U.S. Environmental Protection Agency has established MRLs for cattle meat (0.05 ppm), hog meat (0.05 ppm), pears (3.0 ppm), honey (1.0 ppm), beeswax (6.0 ppm) and cotton seed (1.0 ppm).

## **Value to Agriculture**

### **Description of Market**

Canadian pear production is concentrated mainly in the provinces of B.C., Ontario and Nova Scotia. In the period between 1987 and 1992, pear production in Canada ranged between 18,440 and 27,623 tonnes. Ontario was the largest producer with annual production averaging 12,796 tonnes, or approximately 59% of Canadian production, between 1987 and 1992. B.C. was the second largest producer with annual production averaging 7,830 tonnes, or 35% of Canadian production, in the same period. The average annual production in Nova Scotia during this period was 1,342 tonnes, or 6% of Canadian production.

The annual market value of Canadian pears ranged between \$8.6 million and \$10.7 million between 1987 and 1992. This represents approximately 3.4% of the total farm value of fresh fruit production in Canada.

### **Description of Pest Problem**

Pear psylla (*Psylla pyricola*) is the primary insect pest of pears in North America. Both the adults and nymphs feed on sap from the tree. Feeding by heavy populations of pear psylla can weaken the tree, reduce terminal growth and influence the following season's crop by reducing fruit bud set. Heavy populations of psylla can also cause wilting, scorching and premature leaf drop.

Psylla nymphs produce large amounts of "honey dew", a sap excretion produced during feeding, which accumulates on the leaves and fruit. The smothering effect of this honey dew results in brownish-black patches of dead leaf tissue and a russetting condition on the fruit which downgrades the quality of the fruit at harvest.

Losses from pear psylla result from impacts on fruit quality and quantity. Average grade loss due to pear psylla in B.C. orchards has been estimated to be 20%<sup>1</sup>. This impact on fruit quality can be significant given the often substantial differences in price between extra fancy and lower grades of pears (e.g., over 40¢/kg depending on pear size<sup>2</sup>). Potential yield losses of up to 50% have been estimated due to pear psylla.

### **Control Alternatives**

Pear psylla has developed resistance to most registered chemical treatments. Although the levels of resistance vary among the pear-growing regions in Canada, effective control of pear psylla with available chemical treatments has become increasingly difficult. Reliance of Canadian pear growers on largely ineffective products for control of pear psylla has placed them at a competitive disadvantage vis-à-vis producers in the U.S. and other countries who have access to amitraz and other effective pear psylla pesticides.

In B.C., where no effective insecticide is available for summer control of pear psylla, growers have recently adopted an Integrated Pest Management (IPM) program to preserve natural predators of pear psylla (e.g., mullein bug, anthocorid bugs, lacewings, ladybird beetles). Observations from B.C. orchards in recent years suggest that these natural predators can play a role in maintaining or reducing

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<sup>1</sup> unpublished data from Agriculture and Agri-Food Canada Research Station, Summerland, B.C.

<sup>2</sup> based on prices paid to B.C. growers in 1991 and 1992.

psylla numbers below economic levels. However, an effective insecticide for summer control of pear psylla is required should the population of natural predators fail, or insecticides toxic to predators have to be applied for control of other insect pests (e.g., codling moth, leafrollers).

## **Efficacy**

Published and unpublished reports from field trials conducted in B.C., Ontario and the northwest United States (Washington, Oregon) have shown that post-bloom applications of Mitac WP at a rate of 1.68 - 3.36 kg per hectare significantly reduced populations of pear psylla compared with untreated plots (numbers of pear psylla nymphs were 81% - 99% lower in orchard plots treated with Mitac WP compared with untreated plots).

In most trials, one or two post-bloom applications of Mitac WP at the proposed label rates provided adequate control of pear psylla up to fruit harvest. Post-bloom treatments with Mitac WP were at least as effective, and in most cases significantly more effective, than treatments with currently registered alternatives such as endosulfan, azinphos methyl and synthetic pyrethroids.

The major benefit to pear producers from use of amitraz consists of increased revenue from higher fruit grades and higher realized yields. However, it is difficult to quantify the full extent of the potential monetary returns.

## **Other Product Features**

Amitraz has broad spectrum acaricidal activity and is relatively nonselective to predacious mites such as *Typhlodromus occidentalis*, *Amblyseius fallacis* and mites of the family Stigmaeidae. Users should consult with local pest management specialists regarding proper timing of applications to minimize impact on these beneficial arthropods.

However, the tolerance of pears to phytophagous mites is generally so low that predacious mites rarely provide effective biological control in pears.

## **Human Health Assessment**

Health Canada's previous assessment of the use of amitraz on pears was outlined in *Note to CAPCO C91-01*. In brief, the previously proposed registration would have required the establishment of an MRL of 2.0 ppm on pears. However, the establishment of this MRL was not supported by Health Canada because estimated exposure was expected to exceed the Acceptable Daily Intake (ADI) value in certain sectors of the Canadian population, especially infants and young children. This assessment was based on the expected dietary exposure based on the proposed use pattern and the ADI for the acute effects of amitraz.

Furthermore, Health Canada did not support the registration because there was an inadequate margin of safety for occupational exposure resulting from the proposed use of Mitac WP. The ADI value and the occupational risk assessment were based on an evaluation of all the toxicological and exposure data available at that time.

AgrEvo Canada Inc. has since submitted additional toxicology and exposure data to refine the assessment of the previous ADI and the occupational risk assessment. In addition, the proposed label has been modified to reduce the number of applications and to increase the interval between application and harvest. The following summarizes Health Canada's current assessment of all available information.

## **Toxicology Summary**

Amitraz, an  $\alpha_2$ -adrenergic receptor agonist, manifests its principal effects in laboratory animals and in humans as sedation, hypothermia (decreased body temperature), hypotension (decreased blood pressure) and bradycardia (decreased heart rate). Generally, the acute onset and transient nature of the clinical effects observed with amitraz suggest good correlation between the pharmacological effects of amitraz and plasma concentrations.

A previous comparison of the results from available acute studies with amitraz indicated that man was more sensitive than the dog, the most sensitive laboratory animal species. In a limited metabolic study in man, clinical effects were observed at the single oral dose given of 0.25 mg/kg bw/day, thus a no observable effect level (NOEL) was not demonstrated in man. In the dog, no overt clinical signs of acute toxicity were recorded at a dose level of 0.25 mg/kg bw/day. At the next higher dose level tested (i.e., 1.0 mg/kg bw/day), central nervous system depression, depressed body temperature and depressed pulse rate were noted.

In a recent human study, administration of amitraz at the high dose of 0.125 mg/kg bw/day was without significant clinical effects. This dose level was considered the NOEL for acute effects of amitraz in humans.

The NOEL for amitraz derived from observed acute effects in humans is the lowest among other toxicological endpoints investigated, namely chronic repeated exposure, teratogenicity and reproduction. With regard to carcinogenic potential, the long-term rat study and the initial mouse long-term study were considered negative and there was no evidence of mutagenic potential. The repeat long-term mouse study showed evidence of a tumorigenic response in the livers of the females at the highest dose level, however this was not considered to be biologically significant. Overall, the weight of evidence supports the conclusion that carcinogenicity is not an endpoint for risk assessment.

Based on the results of the recent human study that demonstrated a NOEL of 0.125 mg/kg bw/day for amitraz, the previously estimated ADI of 0.001 mg/kg bw/day for amitraz and the metabolite BTS 27271 has been revised to 0.0125 mg/kg bw/day using a ten-fold safety factor to account for intersubject variability. The ADI for amitraz derived from observed acute effects in humans provides adequate margins of safety with respect to the other toxicological endpoints investigated.

### **Dietary Exposure**

Based on the revised use pattern for Mitac WP, AgrEvo Canada Inc. has proposed an MRL of 1.0 ppm to cover expected residues on treated pears. Residue data provided by AgrEvo Canada Inc. indicate that at the proposed maximum application rate of Mitac WP (i.e., 1.65 kg a.i./ha per application, two applications per season, 14 days between applications, and a 14-day pre-harvest interval), the residues of amitraz plus BTS 27271 on pears did not exceed 0.71 ppm. The MRL of 1.0 ppm is therefore considered adequate to cover the proposed use pattern. This MRL is unlikely to result in an acute exposure exceeding the ADI for any segment of the Canadian population, including infants and young children.

### **Occupational Exposure**

Subsequent to publication of *Note to CAPCO C91-01*, AgrEvo Canada Inc. submitted additional data to assess occupational exposure to amitraz residues from application of Mitac WP to pear orchards. Based on these exposure data, Health Canada still calculates that little or no margin of safety exists for workers wearing standard protective clothing (i.e., long pants, long-sleeved shirt, boots and rubber gloves) during mixing/loading and application of Mitac WP with air-blast equipment.

Given the nature of the pharmacological effect of amitraz, the conservative approach adopted in the study for assessing exposure and pharmacokinetic considerations, Health Canada believes that the low margins of safety calculated to date likely overestimate the risks associated with the use of Mitac WP. However, the extent of the overestimation of the risks cannot be fully determined. In recognition of the likely underestimation of the margins of safety, Health Canada believes that Mitac WP can be used safely if maximum protective measures are followed (see specific recommendations in the following section).

The available data do not allow for an accurate assessment of the safety to workers reentering treated orchards. However, the most stringent precautionary measures possible are recommended for this scenario (see specific recommendations in the following section).

**Health Canada recommended that the following protective measures be followed to reduce exposure to amitraz residues:**

- ! Application should be permitted by ground equipment only. (Due to the lack of exposure data, it is not possible to assess the occupational safety of amitraz applied by aircraft.)
- ! During mixing/loading, application, clean-up and repair activities, individuals should wear a) a chemical resistant suit with a hood over long pants and a long-sleeved shirt, b) a full-face cartridge type respirator or powered-air purifying respirator (“space helmet”), c) chemical resistant gloves, and d) boots. Care should be taken to ensure that all protective equipment and clothing are clean and in good working condition.
- ! The longest interval practically feasible between application and reentry into treated orchards should be observed. The following statement should appear on the label:  
*“Re-entry into treated orchards can result in significant exposure to amitraz residues. Every effort should be made to minimize activity within the orchard and to allow the maximum amount of time practically feasible prior to harvest.”*
- ! Treated orchards should be posted with a sign that reads as follows: “WARNING: Area treated with Mitac WP on (date of application). Do not enter without a long-sleeved shirt, long pants and hat. In case of accidental exposure, see FIRST AID statement on the label.” The sign should remain in place until after harvest.
- ! Growers should ensure that individuals reentering treated orchards are aware of the signs or symptoms of overexposure to amitraz (i.e., skin flushing or rash, drowsiness, dizziness, or decreased heart rate). If any of these signs or symptoms are noticed during handling of Mitac WP or during reentry into treated areas, individuals should stop all work operations. Precautionary statements to this effect should appear on the label.
- ! Mitac WP should be classified as a “RESTRICTED” product, requiring that users be trained and certified by provincial authorities, where applicable. Although no mandatory certification scheme exists in Nova Scotia, grower education courses are available from the province. Users should take such a course.
- ! Mitac WP should be packaged in water soluble packets. Although water soluble packaging is currently not available, AgrEvo Canada Inc. anticipates that such packaging will be available for the 1996 use season.

**Environmental Assessment**

Environment Canada had previously expressed concerns regarding the environmental fate of amitraz and risk to wildlife as presented in *Note to CAPCO C91-01*. AgrEvo Canada Inc. has since amended the use pattern for Mitac WP and has submitted additional data to address these concerns.

The following is a summary of the environmental fate and toxicity of amitraz based on all currently available information:

- ! Based on laboratory data, amitraz is considered to be of low-to-intermediate mobility in fine and medium-textured soils, but may be of higher mobility in coarse-textured soils.
- ! Laboratory studies have indicated that amitraz and its major transformation products BTS 27271 and BTS 27919 are moderately persistent in natural sediment/water. The DT<sub>50</sub> (estimated time for degradation of 50% of the original product) in three types of sediment/water systems ranged from 14 to 32 days at 25°C, and from 48 to 65 days at 8°C.

- ! Results from field dissipation trials conducted in B.C. and Michigan indicate that there is a possibility of accumulation and carryover of amitraz residues.
- ! Amitraz is acutely toxic to aquatic invertebrates and fish (the 48-h LC<sub>50</sub> for the water flea (*Daphnia magna*) is estimated to be 0.035 mg a.i./L; the 96-h LC<sub>50</sub> for rainbow trout (*Oncorhynchus mykiss*) is estimated to be 0.74 mg a.i./L).
- ! Amitraz is not toxic to earthworms (*Lumbricus terrestris*) but is moderately toxic to honeybees (*Apis mellifera*).
- ! BTS 27271 is considered to be of high acaricidal activity. The accumulation and carryover of this bioactive transformation product raises concern regarding the potential negative impact on beneficial non-target organisms in nearby orchard litter (i.e., predatory mites).
- ! Amitraz has low acute toxicity to birds (LD<sub>50</sub> of 788 mg/kg for bobwhite quail (*Colinus virginianus*); LC<sub>50</sub> of 7000 mg/kg-diet for mallard duck (*Anas platyrhynchos*)). Based on recently submitted residue data, there is a potential for dietary chronic toxicity to birds. A risk factor of 0.2 or larger is the criterion chosen to indicate possible concern. Chronic risk factors for amitraz range from 0.5 (bobwhite quail) to 3.8 (wren).
- ! Amitraz is toxic to mammals. The oral LD<sub>50</sub> varies widely with species (100 mg/kg for dog and pig; >100 mg/kg for rabbit; 100-250 mg/kg for baboon; 400-800 mg/kg for guinea pig; 400-940 mg/kg for rat). Based on recently submitted residue data, there is a potential for dietary chronic toxicity to mammals in treated orchards. A risk factor of 0.2 or larger is the criterion chosen to indicate possible concern. Chronic risk factors for amitraz range from 0.3 (rat) to 6.3 (shrew).

However, given the reduction in the application rate, the restricted use pattern and the limited area for pear orchards, exposure will be minimized and it is unlikely that the proposed use of amitraz will adversely affect birds and wild mammals.

Given the reduced concerns regarding impacts on birds and wild mammals, the reduced application rate and the restricted use pattern, data from additional field studies from pear growing regions outside B.C. (e.g., Ontario) are not considered necessary. Furthermore, it is unlikely that these data would provide any substantial new insight into the environmental fate and potential impact of amitraz residues. Based on the Michigan and B.C. field data already available, it is expected that amitraz residues will accumulate and carry over in Ontario.

**Based on the above assessment, Environment Canada has recommended the following regarding use of Mitac WP in pear orchards:**

- ! Mitac WP should not be applied by aircraft.
- ! A buffer zone of 100 metres from water should be observed when applying Mitac WP with an air-blast sprayer.
- ! Caution should be observed when using Mitac WP in an IPM program because of potential negative effects to beneficial non-target organisms (i.e., predatory mites).

**Rationale for Regulatory Decision**

Health Canada has concluded that the residues of amitraz expected on pears following application of Mitac WP according to current label directions do not pose an unacceptable risk to consumers through dietary exposure.

As a result, Health Canada is prepared to establish an MRL, as required under the *Food and Drugs Act*, of 1.0 ppm to accommodate residues of amitraz on treated pears. This MRL will also allow pears containing residues of amitraz up to 1.0 ppm to be imported into Canada.

Based on the available exposure data, Health Canada calculates that there is still little or no margin of safety for workers wearing conventional protective clothing during mixing/loading and application of Mitac WP with an air-blast sprayer. However, because of specific factors involved in the risk assessment, Health Canada believes that the calculated margins of safety likely overestimate the risks associated with the use of this product. As a result, Health Canada believes that Mitac WP can be used safely in pear orchards provided that maximum protective measures are observed.

Results from field dissipation studies indicate that amitraz residues are expected to accumulate and carry over in the soil/orchard litter. Negative impacts on predatory mites, which can be important to IPM programs, may result from both direct spray and exposure to residues. However, adverse effects to birds and wild mammals from exposure to Mitac WP are not anticipated.

In consideration of the identified risks associated with the use of amitraz in pear orchards, and in consideration of the value of Mitac WP to Canadian pear production, Agriculture and Agri-Food Canada, in consultation with Health Canada and Environment Canada, has granted registration until December 31, 1999 to Amitraz Technical (Registration No. 23485) and Mitac WP (Registration No. 23486) for use on pears to control pear psylla.