



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

MAR 25 1994

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Section 18: ID# 94OR0011. Emergency Exemption for Use of ADMIRE 2 Flowable (Imidacloprid) on Hops in Oregon

Tox. Chem. No.: 497E
PC No.: 129099
Barcode No.: D200386
Submission No.: S459672

TO: Rebecca Cool, Manager, PM Team 41
Margarita Collantes, Reviewer, PM Team 41
Emergency Response and Minor Use Section/Registration
Support Branch
Registration Division (H7505C)

FROM: William Dykstra, Ph.D. *William Dykstra 3/17/94*
Review Section I, Toxicology Branch I
Health Effects Division (H7509C)

THRU: Myron S. Ottley, Ph.D. *Myron Ottley 3/17/94*
Review Section IV, Toxicology Branch I
Health Effects Division (H7509C)
and
Roger Gardner, Section Head *Roger Gardner 3/18/94*
Review Section I, Toxicology Branch I
Health Effects Division (H7509C) *KB*

I. CONCLUSIONS

The toxicology data requirements are complete for the issuance of a Section 18 emergency exemption by the State of Oregon for the temporary use of imidacloprid (ADMIRE 2 Flowable) to control aphids on hops. The margins of exposure (MOEs) for acute exposure are greater than 100. Imidacloprid is a "Group E" carcinogen, so there is no cancer risk associated with exposure to this chemical.

Toxicology Branch I has no objection to the issuance of this exemption.

II. ACTION REQUESTED

In a letter dated February 28, 1994, the Oregon Department of



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Agriculture requested an emergency exemption under Section 18 for the use of imidacloprid to control aphids on hops. This is the first request made by Oregon for this use.

ADMIRE 2 Flowable (Miles, Inc.) is the formulation for the active ingredient. The pesticide will be used three times per growing season. The maximum estimated acreage to be treated in Oregon is 8,000. The rate of application will be 6.4 fl. oz. of ADMIRE 2 Flowable per acre (0.1 lb ai) at 21 day intervals. This is equivalent to 1200 lbs of formulated product (2400 lbs ai) for the entire Section 18.

III. TOXICOLOGY BRANCH I COMMENTS

The toxicology data base for imidacloprid is sufficient to support the proposed Section 18 exemption.

IV. RISK/EXPOSURE ASSESSMENT

This action was submitted to OREB (Occupational and Residential Exposure Branch) for determination of exposure estimates (see attached memo from J. Tice to W. Dykstra, dated March 17, 1994). Therefore, the OREB exposure estimates and the rabbit maternal and developmental NOEL of 24 mg/kg/d (see One Liners, below) were used to determine the Acute MOEs. Calculations were based on a dermal absorption of 100%, because no dermal absorption data is available for imidacloprid. Cancer risk is not quantitated, since imidacloprid is a group E carcinogen, and there is no Q₁* for this chemical.

Formula used in calculations:

Acute MOE = NOEL (24 mg/kg BW/d) ÷ Exposure (mg/kg BW/d)

OPERATION*	EXPOSURE (mg/kg/d)	ACUTE MOE
Mixer/Loaders, open pour	0.015	1,600
Applicator, air blast	0.011	2,182

* Minimum clothing requirements for Applicators are long pants, long-sleeved shirt, and chemical resistant gloves; Mixer/Loader exposure is based on wearing long pants, long sleeves, and gloves (Worker Protection Standard for Agricultural Pesticides).

V. SPECIAL TOXICOLOGY ISSUES AND PROBLEMS

1. Labelling. The labelling precautionary statements for ADMIRE 2 Flowable are governed by toxicity studies on the active ingredient.
2. Carcinogenicity. There is no cancer risk associated with exposure to this chemical, because the HED RfD Review

Committee has determined that the test compound is a "Group E" carcinogen.

3. RfD. The RfD/Quality Assurance Peer Review Committee met on April 22, 1993 to assess the reference dose for this chemical. The Committee recommended that an RfD of 0.057 mg/kg/day should be established, based upon a NOEL of 5.7 mg/kg/d in a chronic toxicity study in rats. An uncertainty factor of 100 was used to account for interspecies extrapolation and intraspecies variability.
4. Non-carcinogenic risk assessment. In a chronic/oncogenicity study, male rats exhibited increased thyroid lesions at 16.9 mg/kg/day and above, and females at 73 mg/kg/day (see attached Toxicology Profile, study # 100652/101931). In a developmental study in rabbits, 72 mg/kg/d of technical imidacloprid (administered on days 6-19 of gestation) increased the number of resorptions and abortions in the dams, and increased skeletal abnormalities and decreased body weight in the pups.
5. Mutagenicity/genetic toxicity comments. Most of the genotoxicity studies for imidacloprid were negative, although an in vitro chromosome aberration study (human lymphocytes) was positive at cytotoxic concentrations (Tox. Doc. #099262), and an in vitro sister chromatid exchange mutagenicity study (CHO cells) was positive at cytotoxic doses (Tox. Doc. 102655).
6. Dermal Penetration. There are no available dermal penetration data for imidacloprid. However, a 21 day dermal toxicity study in rabbits has a systemic NOEL of 1000 mg/kg/day (HDT).



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MAR 17 1994

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MEMORANDUM

SUBJECT: Section 18, Oregon State Request to Use Imidacloprid on Hops

FROM: John Tice
Occupational and Residential Exposure Branch
Health Effects Division (H-7509-C)

TO: Bill Dykstra, Ph.D, D.A.B.T.
Toxicology Branch I
Health Effects Division (H-7509-C)

THRU: Mark I. Dow, Ph.D., Section Head
Special Review and Registration Section II
Occupational and Residential Exposure Branch
Health Effects Division (H-7509-C)

Larry Dorsey, Chief
Occupational and Residential Exposure Branch
Health Effects Division (H-7509-C)

Please find below, the OREB review of:

DP Barcode: D-200385

Pesticide Chemical Code: 129099, Imidacloprid

EPA Reg. No.: 3125-UEE, Admire 2 Flowable

EPA MRID No.: N/A

PHED: PHED version 1.01 used for exposure estimates
mixer/loader exposures from run # 7
Air-blast (long-sleeves, pants and gloves) run # 2

REFERRED TO TOX II FOR RISK ASSESSMENT



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I. INTRODUCTION:

Background/Purpose

The State of Oregon has requested an emergency exemption to use Admire 2 F, (imidacloprid) to control mites and aphids on hops. The State of Oregon has 8,000 acres of hops that they feel will need treatment.

II. DETAILED CONSIDERATIONS:

A. Use

Imidacloprid will be applied by ground as a foliar spray at the rate of 6.4 oz product per acre or 0.10 lb ai per acre. A maximum of three applications may be applied per season with a maximum application of 19.2 fl. oz. of product or 0.3 lb ai/acre. Hops are normally grown in rows with 7 ft. centers on trellises that stand approximately 14-18 feet tall. Insecticides are generally applied via ground, air-blast equipment with no less than 100 gallons of water per acre and preferably 400 gallons of water applied per acre for maximum coverage. In discussions with an expert in hops production¹, it is estimated that the maximum acreage that could be sprayed in one day is 20 acres (spraying 20 A would require > 12 hrs.).

B. Toxicology concerns

The tox endpoint of concern is maternal/developmental toxicity with a NOEL of 24 mg/kg/day. Imidacloprid is a tox category III chemical for oral toxicity, dermal and eye irritation; and a tox category IV for inhalation and primary dermal toxicity.

C. Prior exposure reviews

Other exposure evaluations have been performed for hops with the same application rate and same PPE required. The table below provides the estimates of worker exposure.

¹ Personal communications with Dr. Wyatt Cone, Washington State University (IAREC), Prosser, WA (509) 786-2226.

D. Detailed exposure calculations

Exposure calculations are based on the following assumptions:

- Average worker has the mass of 60 kg,
- mixer/loader and applicator can be the same person (see combined exposure),
- respiratory exposure is negligible compared to dermal exposure,
- dermal exposure is not adjusted for dermal absorption,
- standard work clothing is worn which includes protective gloves, long sleeved shirts, long pants, shoes, socks, and hat,
- in one day a single person will mix/load and spray a maximum of 20 acres at 0.1 lbs ai per acre.
- the maximum application rate is used during each of three applications (0.1 lb ai/acre times 3 applications = 0.3 lbs ai/acre per year.)

The following table summarizes daily and annual exposures for mixer/loader, applicator, and mixer/loader/applicator, using an open pour loading system.

WORKER EXPOSURES TO IMIDACLOPRID USING PHED SURROGATE DATA

OPERATION	UNIT EXPOSURE $\mu\text{g/lb handled}$	GROSS EXPOSURE ² 20 ACRES ($\mu\text{g a.i.}$)	DAILY EXPOSURE ³ (20 ACRES) $\mu\text{g/kg}$
M/L OPEN LOAD	448.5	897.0	15.0
GROUND A.B. 20 ACRES	325.9	651.8	10.9
M/L/A GROUND	774.4	1,548.8	25.8

III. CONCLUSIONS:

Daily exposure estimates for a mixer/loader/applicator spraying 20 acres of hops at 0.1 lb ai per acre is 25.8 $\mu\text{g/kg/day}$.

The minimum PPE required include long-sleeved shirt, long pants, shoes with socks, and chemical resistant gloves. Other PPE including chemical resistant headgear, coveralls or rain-suit and dust mist respirator may also be used.

cc: Correspondence File
Imidacloprid File (129099)

² Exposure resulting from handling 2 lbs ai; enough to spray 20 acres @ 0.1 lbs ai/acre.

³ Daily exposure estimate for handling 2 lbs ai. Estimates calculated using the following formula:

$$\frac{\text{Unit Exposure} * (2 \text{ lbs ai})}{60 \text{ kg. bw.}} = \text{Daily Exposure}$$