

US EPA ARCHIVE DOCUMENT

113201

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ECOLOGICAL EFFECTS BRANCH

REVIEW

DATE: IN 5/16/79 OUT 10/10/79

FILE OR REG. NO. 07969-000LG

PETITION OR EXP. PERMIT NO. 9F2205

DATE DIV. RECEIVED 5/1/79

DATE OF SUBMISSION _____

DATE SUBMISSION ACCEPTED _____

TYPE PRODUCT(S): I, D, H, (F), N, R, S Fungicide

DATA ACCESSION NO(S). 098255 and 098256

PRODUCT MGR. NO. (21) Jacoby

PRODUCT NAME(S) Ronilan

COMPANY NAME BASF Wyandotte Corp.

SUBMISSION PURPOSE New chemical/New product - STRAWBERRY EC

CHEMICAL & FORMULATION Vinclozolin; 3-(3,5-Dichlorophenyl)-5-ethenyl-5-

methyl-1,3-oxazolidine-2,4-dione..... 50%

Inerts..... 50%

100%

Vinclozolin
Ronilan (TM)

100 Pesticide Label Information

100.1 Pesticide Use

Vinclozolin (Ronilan TM) is a contact fungicide for the control of botrytis fruit rot on strawberries.

100.2 Formulation Information

Vinclozolin
3-(3,5-Dichlorophenyl)-5-methyl-1,3-oxazolidine-2,4-dione50%
Inerts50%
100%

100.3 Application Methods/Directions/Rates

STRAWBERRIES

Time and Rate of Application: Coverage of the developing fruit is essential. The first application should be made not later than 10% primary bloom at rates recommended below (broadcast basis). The interval between subsequent applications will vary according to weather conditions and resultant disease pressure. If continuous wet periods occur (periods lasting more than 24 hrs.) immediate retreatment is recommended. Then resume the recommended spray schedule.

Rate lb. Product/Acre

<u>Moisture Conditions</u>	<u>Spray* Interval (Days)</u>	<u>1st Year Plants Or Sparse Foliage</u>	<u>Dense Foliage</u>
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FOR ALL AREAS EXCEPT FLORIDA:

Frequent natural moisture (rain, fog, dew) or when using sprinkler irrigation (high disease pressure)	7-9	1.0	1½-2
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Limited natural moisture infrequent sprinkler irrigation (low disease pressure)	10-14	1.0	1½-2
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FOR FLORIDA:

(winter production)	3-5	1.0	1½-2
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*Use spray interval throughout the bearing cycle.

Method of Application: Application of RONILAN should be made in not less than 100 gallons of spray solution per acre to obtain thorough coverage of the developing fruit. An operating pressure of 60-150 psi is recommended to obtain adequate penetration of the spray through the canopy. Cone-type nozzles are recommended. Spray booms with at least 3 nozzles per row (1 over row: 2 side drops) are recommended.

Compatibility: RONILAN is compatible with most fungicides commonly used for anthracnose or leaf scorch such as captan and benomyl. If in doubt, test compatibility with a teaspoon of the other fungicide added to a pint of water.

RESTRICTIONS

Do not apply RONILAN during rain. Wait until conditions are such that the spray will dry on the plants.

Do not apply more than a total of 35 pounds of RONILAN per acre in one season.

100.4 Target Organism

Botrytis fruit rot on strawberries.

100.5 Precautionary Labeling

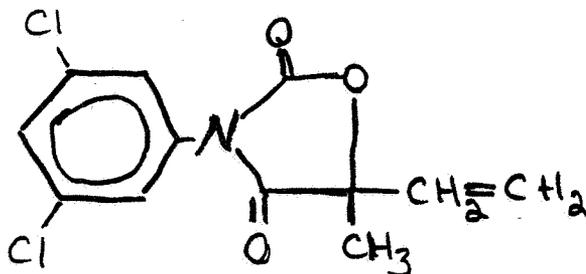
No environmental precautions presented on the label.

101 Physical and Chemical Properties

101.1 Chemical Name

3-(3,5-Dichlorophenyl)-5-ethenyl-5-methyl-1,3-oxazolidone - 2,4-dione

101.2 Structural Formula



101.3 Common Name
 Vinclozolin; BAS 352F

101.4 Trade Name
 Ronilan (TM)

101.5 Molecular Weight
 286.1

101.6 Physical State
 State - solid
 Color - white
 Order - Slight odor, characteristic of aromatic compounds

101.7 Solubility
 (g compound in 100 g solvent at 20°C)

Water	< 0.1
Olive oil	appr. 1.5
Ethyl alcohol	1.4
Acetone	43.5
Ethylacetate	25.3
Cyclohexane	0.9
Ether	6.3
Benzene	14.6
Chloroform	31.9
Iutrol	appr. 2.0

101.8 Hydrolysis

pH	Temperature °C	
	25°	35°
3	70 days	22.5 days
6	61 hrs.	22.5 hrs.
9	12.6 min.	4.8 min.

* Results are for an initial concentration of 1.78 ppm.

At pH's encountered under natural conditions, pH 5-7, (and also at more basic conditions) vinclozolin hydrolyzes mainly to 3,5-dichlorophenylcarbamic acid (1-carboxy-1-methyl) allyl ester (Metabolite B). N-(3,5-dichlorophenyl)-2-methyl-3-butenic acid amide (Metabolite E) is formed mainly at more acidic conditions.

101.9 N-Octanol/Water Partition Coefficient

The n-octanol/water partition coefficient for vinclozolin was found to be approximately 1000. Metabolite B has an n-octanol/water partition coefficient of less than 10.

102 Behavior in the Environment

102.1 Soil

(Note: Taken from Environmental Chemistry EUP review for vinclozolin (RonilanTM) on strawberries; E.B. Brittin, 6/16/78). "Investigation of the Degradation of BAS 352F in Soil." The aerobic study was conducted for 240 days at 20°C on a standard loamy sand (2.5% OM: 40% wet, pH 6.8) spiked with BAS 352F (¹⁴C-phenyl) at 7.0 ppm. The data show about 99.5% of the applied remained after 45 days either bound (38%), as metabolite B (10%), or as extractable parent (37%).

102.2 Water

(Refer to Section 101.8 Hydrolysis).

102.3 Plant

(Note: Taken from Temporary Tolerance and EUP review for vinclozolin (RonilanTM) on strawberries; G.P. Makhijane, 1/19/79.

Residues of vinclozolin on strawberry fruit have a half-life of 3-5 days based on California studies. Results are tabulated below:

Vinclozolin Residues on Strawberry Fruit

	Days after Appl.	Rate (lb AI/Acre)			
		0.25	0.5	1.0	2.0
Residues (in ppm) with single appl.	0	.43	.59	1.7	4.4
	5	.17	.30	.66	2.43
Maximum Residues (in ppm) with Multiple Appls. (12) [every 7-9 days or 10-14 days]	-	1.68	2.90	4.20	7.8

(Note: Taken from Evaluation of Analytical Methodology and Residue Data review for vinclozolin (RonilanTM) on strawberries; M. Nelson, 7/23/79).

Florida studies were conducted at 0.75 lb AI/acre with 21 multiple applications and a 3-7 day spray interval. After the 5th application, residues ranged from 0.47-6.64, depending mainly on the Treatment-to-Sample Interval (TSI). (No other details were given in this review.)

102.4 Animal

(Note: Taken from Temporary Tolerance and EUP review for vinclozolin (RonilanTM) on strawberries; R.A. Gessert, 4/17/78).

METABOLISM; REPEATED ORAL DOSING IN RATS:

Rats (bodyweight ca. 200g) were given daily oral doses of ¹⁴C-labelled vinclozolin for 7 days at ca. 40 mg/kg/day. After daily oral administration of ¹⁴C-vinclozolin to rats, excretion of radioactivity was fairly rapid and was similar in both male and female rats. Approximately 43% and 50% of the daily administered dose were excreted in the urine and feces, respectively, during each day of the dosing period. Six days after the final dose (12 days after the first dose) means of 47% and 54% of the total dose had been excreted in urine and feces, respectively, and means of 0.1% and 0.04% of the total dose were retained in the gastrointestinal tract and liver, respectively. No radioactivity was detected in the remainder of the body at six days after the final dose, nor was any detectable radioactivity excreted in the expired air during 24 hours after the final dose.

A major metabolite in fecal extracts was tentatively identified by mass spectrometry as being N-(3,5-dichlorophenyl)-2-methyl-2,3,4-trihydroxybutyramide. It was also shown that the glucuronide conjugate of this metabolite was the major radioactive component excreted in urine and bile. Unchanged vinclozolin was found in fecal extracts, but not in urine.

103 Toxicological Properties

103.1 References from Toxicology Branch

(Note: Taken from Temporary Tolerance and EUP review for vinclozolin (RonilanTM) on strawberries; R.A. Gessert, 4/17/78.)

Studies Conducted with Technical Material:

ACUTE ORAL TOXICITY, Male & Female Rats: LD₅₀ greater than 10,000 mg/kg

ACUTE INTRAPERITONEAL TOXICITY, Male & Female Guinea Pigs: LD₅₀ = 3,000 mg/kg

ACUTE INTRAPERITONEAL TOXICITY, Male & Female Mice: LD₅₀ = 5,000 mg/kg

TOXIC SYMPTOMS: dyspnea, tremors, spasms, lethargy

POST-MORTEM: hyperemia

ACUTE DERMAL TOXICITY, Male & Female Rats: LD₅₀ greater than 2,500 mg/kg
No toxicity observed

PRIMARY SKIN IRRITATION, Male & Female Rabbits: Primary Skin Irritation Value = 1.3 (moderate)

PRIMARY EYE IRRITATION, Male & Female Rabbits: Primary Eye Irritation Value = 189; no keratitis

Studies Conducted with Formulation:

ACUTE ORAL TOXICITY, Male & Female Rats: LD₅₀ greater than 16,000 mg/kg

ACUTE DERMAL TOXICITY, Male & Female Rabbits: LD₅₀ greater than 2,000 mg/kg

PRIMARY EYE IRRITATION, Female Rabbits: Mean Primary Eye Irritation Score of 19.7;

ACUTE INHALATION TOXICITY IN RAT (dust): No mortality after 4-hour exposure to a dust concentration of 1.17 mg/l, equivalent to 0.59 mg/l active ingredient.

ACUTE INHALATION TOXICITY IN RAT (aqueous spray of 1% suspension): No mortality after 4-hour exposure to a spray concentration of 0.2 mg/liter of air, corresponding to an active ingredient concentration of 0.1 mg/liter of air.

PRIMARY SKIN IRRITATION, Male & Female Rabbits: Primary Skin Irritation Value of formulation = 2.75.

SUBCHRONIC (90 day) TOXICITY IN MALE & FEMALE RATS: No influence at 150 or 450 ppm in feed on standard pathological parameters and measurements. No rats died prematurely. The lowest toxic dose exceeds 450 ppm.

SUBCHRONIC (90 day) TOXICITY IN MALE & FEMALE DOGS: At 100, 300, 1000 or 2000 ppm in feed over a period of 3 months, all doses were tolerated well without externally recognizable symptoms of intoxications. Some histo-chemical effects were observed.

TERATOLOGY (PRENATAL TOXICITY) IN MICE: The compound was administered at levels of 0, 600, 6000 and 60,000 ppm during the entire gestation period. Animals which received 600 and 6000 ppm in their diet did not exhibit any clinically recognizable symptoms to toxicity. Animals receiving 60,000 ppm ate practically none of the food from the first day of the test, and all the animals in this group died within 9 days. The pesticide did not exhibit any teratogenic properties.

3-GENERATION REPRODUCTION STUDY IN RATS: No macroscopic pathological, histological, feeding, growth or reproductive effects were noted in groups fed 0, 162, 486 or 1458 ppm. Treatment began for the 1st (P-) generation 7 weeks before the 1st breeding test and was continued without interruption in all following generations (F₁ -, F₂ -) until the end of the study. The pesticide did not exhibit any teratogenic properties.

CHRONIC TOXICITY AND ONCOGENIC STUDIES: The compound showed no carcinogenic properties in rats fed 162, 486, 1458 and 4375 ppm for 130 weeks, nor in mice fed the same levels for 26 months.

MUTAGENIC EFFECT ON THE MALE MOUSE, USING THE DOMINANT LETHAL TEST: 2000 mg/kg was administered on 5 successive days via stomach tube in 20 ml/kg 0.5% aqueous CMC formulation. Control animals received only the CMC formulation. There were no clinically recognizable symptoms of toxicity, and no evidence of any effect on conception rate, average number of implants, percentage of viable fetuses, or percentage of dead implants. Under conditions of the test, the compound could not be shown to have any mutagenic effect on male mice.

103.2 Minimum Requirements

103.2.1 Avian Acute Oral LD₅₀

Bobwhite quail (Colinus virginianus)

LD₅₀ >>2150 mg/kg - (96.5%)

Wildl. Interntl. Ltd. (1978)

Core - Felthousen (7/24/78)

(Pestic. Pet. 9F2205, Book 3; Acc. No. 098255: Rept. I-1).

103.2.2 Avian Dietary LC₅₀'s

Bobwhite quail (Colinus virginianus)

LC₅₀ >>5620 ppm - (96.5%)

Fink and Beavers, 1978 (Wildl. Interntl.)

Core - Balcomb (5/9/78)

(Pestic. Pet. 9F2205, Book 3: Acc. No. 098255, Rept. I-2).

Mallard (Anas platyrhynchos)

LC₅₀ >>5620 ppm - (96.5%)

Wildl. Internatl. Ltd. (1978)

Core - Felthousen (7/24/78)

(Pestic. Pet. 9F2205, Book 3; Acc. No. 098255, Rept. I-3).

103.2.3 Fish Acute LC₅₀'s

Bluegill (Lepomis macrochirus)

96-hr LC₅₀ = 47.3 (37.1-60.3) (96.5%, resubmitted for this review)

Calmbacher, 1978 (UCES)

Supplemental - Balcomb (5/9/78)

(Pestic. Pet. 9F2205, Book 3; Acc. No. 098255, Rept. I-4).

Rainbow trout (Salmo gairdneri)

96-hr LC₅₀ = 18.0 ppm - (96.5%, resubmitted for this review)

Calmbacher, 1978 (UCES)

Supplemental - Balcomb (5/9/78)

(Pestic. Pet. 9F2205, Book 3; Acc. No. 098255, Rept. I-6).

103.2.4 Aquatic Invertebrate LC₅₀

Daphnia magna

48-hr LC₅₀ = 4.0 ppm - (96.5%)

Union Carbide Environ. Serv. (1978)

Core - Felthousen (7/24/78)

(Pestic. Pet. 9F2205, Book 3; Acc. No. 098255, Rept. I-8).

103.4 Additional Aquatic Laboratory Studies

Note: The following are not validations.

Bluegill - Metabolite B of vinclozolin - (99.5%)

96-hr LC₅₀ = 135.4 ppm

Calmbacher, 1978 (UCES)

(Pestic. Pet. 9F2205, Book 3; Acc. No. 098255; Rept. I-5).

Rainbow trout - Metabolite B of vinclozolin - (99.5%)

96-hr LC₅₀ = 80.6 (71.8-90.5) ppm

Calmbacher, 1978 (UCES)

(Pestic. Pet. 9F2205, Book 3; Acc. No. 098255; Rept. I-7).

Daphnia magna - Metabolite B of vinclozolin - (99.5%)

48-hr. LC₅₀ = 79.7 (64.1-99.1) ppm

Morrissey, 1978 (UCES)

Pestic. Pet. 9F2205, Book 3; Acc. No. 098255; Rept. I-9).

104 Hazard Assessment

104.1 Discussion

Vinclozolin is applied at ½-1 lb AI/acre (1-2 lb formulation/acre) with the nozzles of the ground spray equipment arranged to concentrate the spray on the plants. Spray intervals are 7-9

days for high disease pressure, 10-14 days for low disease pressure, and 3-5 days for Florida only. Not more than 17½ lb AI/acre is allowed in one season. The first application should be made no later than 10% bloom.

Vinclozolin has a half-life of 3-5 days on strawberry fruit. It is relatively soluble in water and hydrolyzes with a half-life of 61 hrs at 25°C and pH 6. Its major degradate is Metabolite B. The n-octanol/water partition coefficients for parent and metabolite are 1000 and less than 10, respectively.

Balcomb (5/9/78) estimated residues on strawberries fruits and leaves at 1 lb/acre at 7 and 58 ppm, respectively; assuming that the pesticide is concentrated on 60% of each acre, estimated fruit residues were 11.6 ppm. In California field studies, initial fruit residues after one application at 2 lb/acre were 1.7 ppm; however, maximum residues with multiple applications were 4.2 ppm. In Florida field studies, maximum residues with multiple applications at 0.75 lb/acre were 6.64 ppm; assuming a linear relationship between increasing rate and increasing residues, at 1 lb/acre residues can be 8.85 ppm (6.64 x 1.333).

104.2 Likelihood of Adverse Effects

Aquatic Organisms

Exposure of aquatic organisms to vinclozolin is unlikely considering that sprays are close to and directed at plants and the hydrolytic half-life of the compound. While it is moderately toxic to aquatic invertebrates (48-hr LC₅₀ = 4.0 ppm) and has some potential for bioaccumulation (partition coeff. = 1000), its degradate is only slightly toxic (48-hr LC₅₀ = 79.7 ppm) and is unlikely to bioaccumulate in fatty tissues (partition coeff. 10). Therefore, no adverse effects are expected on aquatic organisms.

Wildlife

As noted by Balcomb (5/9/78), while some exposure is likely to occur, the acute hazard is low. However, vinclozolin is applied on strawberries from 10% bloom until harvest, a period of about 2 months. Thus, there is the potential for chronic and reproductive effects on wildlife.

104.3 Endangered Species Considerations

No acute hazard anticipated.

104.4 Adequacy of Toxicity Data

The following studies have been validated as Core and are considered adequate to support the registration of Ronilan^(TM) (vinclozolin) for use as a fungicide on strawberries.

1. Avian acute oral LD₅₀
-Bobwhite quail; Wildl. Interntl. Ltd. (1978);
Felthousen (7/24/78)
2. Avian dietary LC₅₀'s
 - a. Bobwhite quail; Fink and Beavers (1978); Balcomb (5/9/78)
 - b. Mallard; Wildl. Interntl. Ltd. (1978); Felthousen (7/24/78)
3. Aquatic invertebrate LC₅₀
-Daphnia magna; UCES (1978); Felthousen (7/24/78)

The following studies have been validated as Supplemental and are not considered adequate to support the registration of Ronilan^(TM) (vinclozolin):

Fish acute LC₅₀'s

- Bluegill; Calmbacher (1978)
- Rainbow trout; Calmbacher (1978)
- Balcomb (5/9/78) - Objections originally noted were: percent active ingredient not given, and (in the rainbow trout study) lack of adequate dissolution of test material, as evidenced by the presence of white flocculent material above 18 ppm, resulting in inadequate dose-response data. The original reviewer concluded: 1) the rainbow trout study must be redone with a solvent other than that used (acetone), and 2) the bluegill study "will be reconsidered" when the registrant submits the percent active ingredient.

The registrant has given the percent active ingredient with this submission. However, upon reconsidering the bluegill study, both this and the original reviewer (R. Balcomb) note that a lack of adequate dissolution of test material in this study as well, as evidenced by the presence of white flocculent material at all concentrations (5.6 to 56 ppm). Therefore, the bluegill study must be redone as well with a solvent other than that used (acetone).

104.5 Additional Data Required

The following required studies must be redone with a solvent other than that used originally (acetone):

- Fish acute LC₅₀'s - 96-hr
- Warmwater (preferably bluegill)
- Coldwater (preferably rainbow trout)

The following studies are also required prior to consideration of registration of vinclozolin on strawberries:

Avian reproduction

- Mallard
- Bobwhite quail

Note: Appropriate test levels for the avian reproduction test will depend upon both current and future registration submissions. Therefore, the registrant may wish to contact EEB to help determine appropriate test levels for the current strawberry submission as well as possible future submissions.

107 Conclusions

107.3 Environmental Hazards Labeling

Since the submitted and referenced data are insufficient for EEB to complete its Hazard Assessment, what proper environmental hazard cautions should appear on the label cannot be addressed at this time.

107.4 Data Adequacy Conclusions

The following studies have been validated as Acceptable to support the registration of Ronilan^(TM) (vinclozolin) for use as a fungicide on strawberries.

1. Avian acute oral LD₅₀ - Bobwhite quail; Wildl. Interntl. Ltd. (1978).
2. Avian dietary LC₅₀'s - Bobwhite quail; Fink and Beavers (1978) - Mallard; Wildl. Interntl. Ltd. (1978).
3. Aquatic invertebrate LC₅₀ - Daphnia magna; UCES (1978).

The following studies have been validated as Unacceptable to support registration of Ronilan^(TM):

Fish acute LC₅₀'s - Bluegill & Rainbow trout; Calmbacher (1978).

Objections found upon reconsidering the bluegill study and noted originally by R. Balcomb (5/9/78) for the rainbow trout is a lack of adequate dissolution of test material as evidenced by the presence of white flocculent at most concentrations.

107.5 Data Requests

The following required study must be redone with a solvent other than that originally used (acetone):

Fish acute LC₅₀'s - 96-hr

- Warmwater (preferably bluegill)
- Coldwater (preferably rainbow trout)

The following studies are also required prior to consideration of registration of Ronilan^(TM) on strawberries:

Avian reproduction

- Mallard
- Bobwhite quail

Note: Appropriate test levels for the avian reproduction test will depend upon both current and future registration submissions. Therefore, the registrant may wish to contact EEB to help determine appropriate test levels for the current strawberry submission as well as future submissions on additional crops.

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