DIRS 5-14-97

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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

DATE: 5/14/97

SUBJECT: **PP# 9F03762.** SECTION 3 REGISTRATION AND TOLERANCE PETITION FOR USE OF **VINCLOZOLIN** ON **SNAP BEANS.**

DP Barcodes: D233000, D233043, D233176, D235556
Caswell: 323C
Trade Name: RONILAN® DF (Reg.# 7696-85)
Chem#: 113201
Case#: 280803, 044332
Class: fungicide
40 CFR: 180.380; 185.1850; 186.1850
MRID#s: 435059-03 and 442627-01

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INTRODUCTION

The registrant, BASF, is requesting a Section 3 registration and establishment of a tolerance for use of vinclozolin on snap beans to control white mold (Sclerotinia sclerotiorum) and grey mold (Botrytis cinerea).

BACKGROUND

In the process of reviewing this petition and conducting associated risk assessments, a meeting was held with the registrant at which the registrant indicated a desire to amend or delete certain registered uses of vinclozolin. These are noted appropriately in the body of the text. **If these changes are not made, another risk assessment will need to be conducted.**

RECOMMENDATION

- Provided that the label changes are made as outlined below, occupational risk estimates do not exceed HED's level of concern.

- Provided that the label and CFR changes are made as noted below, aggregate acute, chronic, and cancer risk estimates do not exceed HED's level of concern.

- **Currently, aggregate short-term risk estimates exceed HED's level of concern. However, if all residential uses of vinclozolin are canceled, the aggregate short-term risk estimates will not exceed HED's level of concern.** Based on the severity and nature of the toxic endpoint (single hit, non-reversible), PIRAT recommends that a non-occupational MOE of 100 be met. In order to achieve this, all residential uses of vinclozolin need to be canceled.

Label Changes

Occupational Exposure

The label provided with the submission [RONILAN® DF (Reg.# 7696-85)] proposes an re-entry interval (REI) of 12 hours for snap beans. Based on extrapolation from a strawberry foliar dislodgeable residue study (FDR), the REI for snap beans should be 3 days. The REI may be changed pending receipt and review of an acceptable FDR study for snap beans per se.

- **A revised Section B should be submitted specifying a 3-day REI for snap beans.**

For aerial application, the RONILAN® DF label states "use less than 20 gallons of spray solution per acre". The minimum spray solution for aerial application should be no less than 5 gal/A.

- **A revised Section B should be submitted limiting aerial application to no less than 5 gallons per acre.**

With the current submission on snap beans, BASF originally proposed that all three of their vinclozolin formulations [RONILAN® DF (Reg.# 7696-85), RONILAN® WP (Reg.# 7696-53), and/or RONILAN® FL (Reg.# 7696-62)] would be used on snap beans, but later modified their request to specify the DF formulation only.

- **HED recommends that RD insure that only the RONILAN® DF (Reg.# 7696-85) formulation is to be registered for use on snap beans.**

A second company, Scotts-Sierra Crop Protection Co, has a product containing vinclozolin (EPA Reg. No. 58185-17) that is currently registered for use on ornamental flowering plants and ornamental turf. Scotts-Sierra is an end-use formulator of vinclozolin.

- **HED recommends that RD insure that any residential use restrictions placed on the RONILAN® DF product also apply to the Scotts-Sierra product.**

Residue Chemistry

Issues surrounding the need for rotational crop tolerances have not been resolved. As part of the reregistration process, BASF has been advised that they need to conduct a new study to fulfill Guideline 165-1 data requirements. In the interim, the proposed label should be changed to limit rotation within 12 months to crops which have tolerances with U.S. registrations.

- **A revised Section B should be submitted which restricts rotation to the following non-tree crops: caneberries, garlic, onions, lettuce, shallots, and strawberries.**

RD should insure that any references to use of any vinclozolin [RONILAN® DF (Reg.# 7696-85), RONILAN® WP (Reg.# 7696-53), and/or RONILAN® FL (Reg.# 7696-62)] formulation on Belgian endive, cucumbers, grapes, kiwifruit, and peppers **is removed.** BASF has indicated that these sites are only foreign uses (no U.S. Registration). The dietary risk assessments presented in this memo assumed only foreign and no domestic use of vinclozolin on these commodities (i.e., all imports were assumed to have regulable residues).

- **HED recommends that RD insure that no vinclozolin-containing products list the following use sites: Belgian endive, cucumbers, grapes, kiwifruit, and/or peppers.**

In the Section F with the current submission, BASF has proposed a 3.0 ppm tolerance for snap beans. This tolerance level was based on an application rate 2 times higher than

that currently sought (1.0 lb ai/A/application, and 14 day-PHI versus 0.5 lb ai/A/application, and 9 day PHI).

- **A revised Section F should be submitted which proposes a 2.0 ppm tolerance for regulable residues of vinclozolin on snap beans.** This level harmonizes the US tolerance with the CODEX MRL and in the best scientific judgement of PIRAT is supported by available field trial residue data (see Additional Information, Tables 11 and 12 for detailed discussion)

CFR Changes

Since the values below were used in the dietary risk asessments, PIRAT recommends that the current 40 CFR 180.380 be amended to appear as follows:

commodity	tolerance (ppm)
Belgian endive, tops	2.0[1]
Beans, snap	2.0
Caneberries, except raspberries	10.0[2]
Cranberries	2.0[3]
Cucumbers	1.0
Grapes, wine	6.0[4]

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[1] The current tolerance is 5 ppm. In the Chemistry Chapter of the RED, CBTS recommended that this tolerance be decreased to 2.0 ppm (see memos of S. Knizner dated 10/4/95 and 11/15/95. In a memo of J.Smith dated 9/17/91 (DP Barcodes D166259, D166245, and D166246), the established "import" tolerance in/on Belgian endive was extended to include domestically produced Belgian endive tops. However, BASF wishes to keep this as a tolerance with no U.S. registration (communication with Dr. Abraham Tobia in a meeting held on 4/17/97). The risk assessment was conducted assuming only imported Belgian endive tops would contain residues of vinclozolin, and a 2.0 ppm tolerance was used for chronic dietary risk.

[2] This tolerance is not currently listed in 40 CFR 180.380, but CBTS recommended in favor of this tolerance in PP#0F3903. This tolerance was used in the chronic dietary risk assessment. EFED considerations permitting, this tolerance should be established.

[3] This tolerance is not currently listed in 40 CFR 180.380, but CBTS recommended in favor of the tolerance in PP#4E4377 (memo of S. Willett dated 11/9/94). The risk assessments assumed residues of vinclozolin would be found in cranberries. EFED considerations permitting, this tolerance should be established.

[4] The current tolerance of 6.0 ppm listed in 40 CFR 180.380 is designated to apply to all grapes. This tolerance was originally established to apply to imported grapes only (no U.S.

commodity	tolerance (ppm)
Kiwifruit	10.0
Lettuce, head	10.0
Lettuce, leaf	10.0
Onions, dry bulb	6.0[5]
Peppers, bell	3.0
Raspberries	5.0[6]
Stonefruits, except plums/prunes	5.0[7]
Strawberries	10.0

- **Language should be added to 40 CFR 180.380 specifying that "There are no U.S. registrations for Belgian endive, cucumbers, grapes (wine), kiwifruit, and peppers as of 05/12/97".**

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registration). However, BASF wishes to change this tolerance to apply to imported wine grapes (i.e. imported wine) only (communication with Dr. Abraham Tobia in a meeting held on 4/17/97). The only grape-related commodities which were used in the dietary risk assessments for vinclozolin were wine/sherry.

[5] The current tolerance listed in 40 CFR 180.380 is 1.0 ppm. However, due to overtolerance residues, CBRS recommended that this tolerance be changed to 6.0 ppm (memo of F. Fort dated 9/23/93 - DP Barcode D187397). The 6.0 ppm tolerance was used in the chronic risk assessment and the "over tolerance" field trial results, along with all other field trial results which supported the labeled use, were incorporated into the acute Monte Carlo risk assessment.

[6] The current raspberry tolerance is 10.0 ppm. In the Chemistry Chapter of the RED, CBRS recommended that this tolerance be decreased to 5.0 ppm (see memos of S. Knizner dated 10/4/95 and 11/15/95). The 5 ppm tolerance was used in the chronic dietary risk assessment.

[7] The current stonefruit tolerance is 25 ppm. However, in the Chemistry Chapter of the RED, CBRS recommended that this tolerance be reduced to 5.0 ppm (memos of S. Knizner dated 10/4/95 and 11/15/95). Currently, BASF wishes to omit plums/prunes from the stonefruit crop group (communication with Dr. Abraham Tobia in a meeting held on 4/17/97). The risk assessments were conducted assuming both of these changes.

The following crops/commodities should be deleted from the Federal Register:

40 CFR 180.380

Tomatoes

The 3.0 ppm tomato tolerance that currently appears in the CFR was originally established to apply to imported tomatoes only (no U.S. Registration). However, BASF wishes to drop this tolerance and not market the product for use on tomatoes outside of the U.S. (communication with Dr. Abraham Tobias in a meeting held on 4/17/97). Tomatoes and related products were not used in conducting the acute and chronic risk assessments for vinclozolin.

- **HED recommends that RD insure that the 3 ppm tolerance on tomatoes is revoked.**

- **PIRAT notes that it is especially important that RD insure that the tomato tolerance is removed from 40 CFR 180.380. Since this is an "import" tolerance (i.e. no U.S. Registration), until the 3.0 ppm tolerance is revoked, treated tomatoes can legally be imported into the U.S.**

40 CFR 185.1850

All entries should be deleted.

Prunes

BASF wishes to omit plums/prunes from the stonefruit crop group (communication with Dr. Abraham Tobias in a meeting held on 4/17/97). Prunes were not used in conducting the acute and chronic risk assessments for vinclozolin.

- **HED recommends that RD insure that the 75 ppm tolerance on prunes is revoked and the use on plums deleted from all of the Section 3 labels.**

Raisins

BASF wishes to modify the existing 6.0 ppm "import" tolerance on all grapes to apply to imported wine grapes (i.e. imported wine) only (communication with Dr. Abraham Tobias in a meeting held on 4/17/97). Raisins were not used in conducting the acute and chronic risk assessments for vinclozolin.

- **HED recommends that RD insure that the 30 ppm tolerance on raisins is revoked.**

40 CFR 186.1850

All entries should be deleted.

Grape Pomace, dry

This tolerance should be revoked for the reasons stated above for raisins. Also, grape pomace is no longer recognized as a significant animal feed item in Table 1 of OPPTS 860.1000. Grape pomace was not used in conducting the acute and chronic risk assessments for vinclozolin.

- **HED recommends that RD insure that the 42 ppm tolerance on dry grape pomace is revoked.**

Pending Tolerances

While CBTS recommended in favor of the establishment of a 4.0 ppm tolerance on blueberries (PP#0E3850), BASF does not want this use included in the current risk assessments (communication with Dr. Abraham Tobias in a meeting held on 4/17/97). Therefore, this tolerance should not be established at this time.

Note to P.M.: RD should insure that any kiwifruit 24(c) registrations, including CA (CA83004400) and SC (SC90000500 and SC90000600), are revoked. These 24(c) registrations are not supported by U.S. field trial residue data. Further, BASF concurs that the kiwifruit tolerance should be designated as "import" only (no U.S. Registration).

- **HED recommends that RD rescind the following SLN registrations: CA83004400, SC90000500, and SC90000600.**

RISK CHARACTERIZATION

Occupational Exposure Assessment

The occupational risk assessment for vinclozolin was conducted using PHED (Pesticide Handlers Exposure Database) and Best Available Surrogate Exposure Table (BASET, 7/25/96). The risk to mixer/loaders is somewhat conservative because the label requires additional PPE (chemical-resistant apron). However, additional refinement is not possible in the absence of actual exposure data.

- **Provided that the changes outlined under the RECOMMENDATION section of this memo are made, in the best scientific judgement of HED, the vinclozolin worker risk from this Section 3 registration on snap beans does not exceed our level of concern.**

Acute Aggregate Risk Assessment

The acute dietary (food only) risk assessment used Monte Carlo analysis and percent of crop treated or percent imported data for selected commodities (apricots, beans, raspberries, cherries, cucumbers, lettuce, nectarines, onions, peaches, peppers, and strawberries.), while other commodities were assumed to be 100% treated/imported (caneberries, other than raspberries; cranberries; endive; garlic; wine/sherry; kiwifruit; and shallots). Tier 2 anticipated residue refinement was performed for the mixed commodity wine/sherry. **For imported**, single-serving commodities, acute anticipated residue refinement was performed by using the highest field trial value in the Monte Carlo analysis. For all commodities which have a corresponding Section 3 registration, the Monte Carlo analysis used the full range of field trial residue data which reflected the existing (or proposed) use directions.

For the subgroup of concern, females 13+ years, the resulting high-end (99.9th percentile) dietary (food only) exposure estimate of 0.013587 mg/kg/day, when added to the surface water exposure estimate of 0.0009013 mg/kg/day, results in a dietary (food + water) MOE of 380. This estimate should be viewed as a refined risk estimate; further refinement using additional percent of crop treated or percent imported data may result in a slightly lower acute dietary exposure estimate. The acute surface water exposure value is based on modeling and should be viewed as a worst-case, upper-bound value. However, further refinement of this value would have a small effect on the aggregate acute risk (food + water), because the exposure contribution from drinking water is very small compared to dietary food exposure.

- **Provided that all of the changes outlined under the RECOMMENDATION section of this memo are made, in the best scientific judgement of HED, the vinclozolin aggregate acute risk (food and water) from the currently registered uses and this Section 3 registration on snap beans does not exceed our level of concern.**

Chronic Aggregate Risk Assessment

The chronic dietary (food only) risk assessment used percent of crop treated or percent imported data to refine the risk estimate for selected commodities (apricots, beans, raspberries, cherries, cucumbers, lettuce, nectarines, onions, peaches, peppers, and strawberries), while other commodities were assumed to be 100% treated/imported (caneberries, other than raspberries; cranberries; endive; garlic; wine/sherry; kiwifruit; and shallots). No chronic anticipated residue refinement has been performed. Therefore, the resulting exposure (food only) estimates should be viewed as partially refined; further refinement using anticipated residues and additional percent of crop treated/percent imported data would result in lower dietary exposure estimates. The chronic surface

water exposure value is based on modeling and should be viewed as a worst-case, upper-bound value. However, further refinement of this value would have a small effect on the total risk (food + water), since the contribution from drinking water is very small compared to food. Other than dietary exposure, no chronic exposure scenarios have been identified from registered uses of vinclozolin. For chronic dietary (food + water) risk estimates, the population subgroup with the largest percentage of the RfD occupied is U.S. Population, Western Region at 16% of the RfD.

- **Provided that all of the changes outlined under the RECOMMENDATION section of this memo are made, in the best scientific judgement of HED, the vinclozolin aggregate chronic risk (food and water) from the currently registered uses and this Section 3 registration on snap beans does not exceed our level of concern.**

Short- and Intermediate-Term Aggregate Risk Assessment

Short-term risk was estimated to exceed HED's level of concern as shown in Tables 3 and 6 of this memo. Table 3 presents the results of aggregating the chronic dietary exposure (Table 1) with the short-term exposure resulting from turf use (Exposure Scenario 2). The chronic dietary exposure estimates should be viewed as partially refined for the reasons mentioned above. However, the dietary portion of the estimated risk is relatively insignificant; the aggregate risk is driven by the turf exposure outlined in Exposure Scenario 2. As noted in the Uncertainties Surrounding Scenario 2, PIRAT believes that, based on available data, the exposure estimates are partially refined, but further refinement would not achieve an MOE above 100.

- **Aggregate short-term risk estimates for vinclozolin, which include exposure resulting from residential turf use, exceed HED's level of concern.**

Table 6 presents the results of aggregating the chronic dietary exposure (Table 1) with the short-term exposure from the homeowner mixer/loader/applicator (Exposure Scenario 1) and the short-term postapplication dermal exposure from vinclozolin-treated home gardens and orchards (food and/or ornamentals), as outlined in Exposure Scenario 3. Current HED policy for calculating short-term aggregate exposure is to add chronic dietary exposure (considered to be background exposure level) to any indoor and/or outdoor residential exposure. However, in this case, use of chronic dietary exposure levels may underestimate the risk. If the homeowner were to mix/load/apply the product, it would be in his or her own yard and could involve application to food crops and/or ornamentals. If it were applied to food crops near harvest (for homeowner use, OREB policy is to assume a 0-day PHI), that produce would typically be consumed by the homeowner (and his or her family), **and the produce would be 100% crop treated.** Therefore, in

the short-term time period, the person may potentially receive exposure from mixing/loading/applying the pesticide, post-application dermal exposure to the chemical, and food exposure levels that resemble acute exposure, more than chronic exposure. Using this scenario, **and ignoring any contribution from drinking water**, the total exposure for the subgroup U.S. Population would be homeowner handler (0.016 mg/kg/day) + home garden post-application exposure (0.023 mg/kg/day) + acute dietary (0.013587 mg/kg/day) = 0.053 mg/kg/day. Using the short-term NOEL of 3 mg/kg/day, **the calculated MOE is 57** (using chronic food and water, this estimate is 74, as shown in Table 6).

As noted under Uncertainties Surrounding Exposure Scenario 1 (Homeowner Handler Exposure), the handler data are taken from PHED, and therefore may underestimate exposure to a homeowner who is likely to be less skilled in pesticide mixing, loading, and application methods, have access to less sophisticated equipment, and be less knowledgeable about general safe practices for handling pesticides. Scenario 3, may overestimate risk, since the scenario is drawn from studies of workers harvesting produce as wage earners, and extrapolated back to an estimated 2 hours spent picking or coming in contact with vinclozolin-treated ornamentals in the home garden.

PIRAT believes that, even with additional exposure refinement, the MOEs presented in Table 6 of this memo for subpopulations 13 years of age and older, would not equal or exceed 100.

- **Aggregate short-term risk estimates for vinclozolin, which include homeowner use on ornamentals and food crops, exceed HED's level of concern.**

- **Provided that all residential uses of all formulations of vinclozolin are canceled, the aggregate short-term risk estimates will not exceed HED's level of concern.**

Cancer Aggregate Risk Assessment

The Cancer Peer Review Committee (CPRC) met on 1/15/97 (3rd Meeting, memo dated 4/3/97), and recommended that vinclozolin should be classified as Group C chemical - possible human carcinogen, with a non-linear approach (MOE) based on a NOEL of 4.9 mg/kg/day for hormone-related effects (decreased epididymal weight at 30 mg/kg/day) in the 2-generation oral reproductive toxicity study in rats to quantify human risk.

The Anticipated Residue Contribution (ARC) from the chronic DRES analysis for the U.S. Population was calculated to be 0.001383 mg/kg/day from food and 0.0000303 from dietary water, for a total dietary exposure (food + water) of 0.001413. Using the formula where the Margin of Exposure (MOE) = NOEL (mg/kg/day) ÷ Exposure (mg/kg/day), or 4.9 mg/kg/day ÷ 0.001413 mg/kg/day, the calculated

MOE (food only) is 3,500. Other than dietary exposure, no chronic exposure scenarios have been identified from registered uses of vinclozolin.

- **Provided that all of the changes outlined under the RECOMMENDATION section of this memo are made, in the best scientific judgement of HED, the vinclozolin aggregate cancer risk (food and water) from the currently registered uses and this Section 3 registration on snap beans does not exceed our level of concern.**

CONCLUSIONS

Hazard Assessment

1. Non-Dietary Exposure Endpoint Selection

a) Short- and Intermediate-Term Risk for Females Age 13 and Older. For short- and intermediate-term MOE calculations, the TES Committee [7/18/96] recommended the use of an oral rat developmental toxicity study (Gray et al., 1993). The developmental NOEL was 3 mg/kg/day and the LOEL was 6.0 mg/kg/day based on the occurrence of pseudohermaphroditism (reduced anogenital distance) in male fetuses and nipple development. The maternal toxicity NOEL/LOEL were also 3 and 6 mg/kg/day, respectively in this study and were based on reduced sex organ weights.

b) Short- and Intermediate-Term Risk for Infants and Children Ages 1-12. For short- and intermediate-term MOE calculations for infants and children ages 1-12, the Ad Hoc TES Committee [memo of 4/30/97 from D. Anderson - see Attachment I] recommended the use of a NOEL of 5.0 mg/kg/day from an oral rat study based on delayed puberty in young rats at the LOEL of 15 mg/kg/day. This endpoint is based on data presented by Earl Gray at the 1996 Science Advisory Panel (SAP) meeting discussing vinclozolin.

c) Chronic Risk. A chronic risk exposure scenario has not been identified for the proposed use, although the chronic TES endpoint is based on the NOEL [1.2 mg/kg/day] for the RfD.

d) Cancer Risk. The Cancer Peer Review Committee [CPRC] met on 1/15/97 (3rd Meeting, memo dated 4/3/97) to re-evaluate the carcinogenic potential of vinclozolin, based on revised pathology results. The majority of the CPRC agreed that vinclozolin should be classified as Group C chemical - possible human carcinogen. This classification was based on the statistically significant

increase in Leydig cell tumors in the rat; although, some members felt that the increases in prostate tumors were equivocal, but could not be dismissed since there were no prostate tumors in concurrent controls. The Committee chose a non-linear approach [MOE] based on a NOEL of 4.9 mg/kg/day for hormone-related effects [decreased epididymal weight at 30 mg/kg/day] in the 2-generation oral rat reproductive toxicity study to quantify human risk. The MOE approach was chosen because the remaining tumors [Leydig cell] were benign at dose levels which were not considered to be excessive, and there was little concern for mutagenicity of vinclozolin.

e) Dermal Penetration. Dermal penetration of 25% has been determined in a rat dermal penetration study (MRID# 41824309).

2. Dietary Endpoint Selection

a) Acute Risk = 5.5 mg/kg/day. For acute dietary risk assessment, the TES Committee recommended the use of the NOEL of 5.5 mg/kg/day in a rat developmental toxicity study (Gray et al., 1993) for evaluating acute risks to females 13+ years, based on several considerations and the oral rat developmental toxicity study findings (Gray et al., 1993). The dose of 5.5 mg/kg/day was calculated by HED using the bracketed conversion (3 mg/kg/day X 3.91/2.12 = 3 X 1.8 = 5.5 mg/kg/day), in order to obtain the **single day** internal dose corresponding to 3 mg/kg in rats from dosing on multiple days.

b) Chronic Risk. RfD = 0.012 mg/kg/day. An RfD of 0.012 mg/kg/day was established based on a 2-year rat feeding study with a NOEL of 1.2 mg/kg/day and a uncertainty factor of 100. At the LEL of 2.4 mg/kg/day, there were cataracts, ovarian lipidosis, and fatty liver changes in females and foam cell aggregates in the lungs, eosinophilic altered liver foci, and adrenal cortical focal hyperplasia in males. Based on the 2/21/97 memo of William Burnam, additional modifying factors to the RfD due to developmental findings are not appropriate.

c) Cancer Risk. The Cancer Peer Review Committee [CPRC] met on 1/15/97 (3rd Meeting, memo dated 4/3/97) to re-evaluate the carcinogenic potential of vinclozolin, based on revised pathology results. The majority of the CPRC agreed that vinclozolin should be classified as Group C chemical - possible human carcinogen. This classification was based on the statistically significant increase in Leydig cell tumors in the rat; although, some members felt that the increases in prostate tumors were equivocal, but could not be dismissed since there were no

prostate tumors in concurrent controls. The Committee chose a non-linear approach [MOE] based on a NOEL of 4.9 mg/kg/day for hormone-related effects [decreased epididymal weight at 30 mg/kg/day] in the 2-generation oral rat reproductive toxicity study to quantify human risk: The MOE approach was chosen because the remaining tumors [Leydig cell] were benign at dose levels which were not considered to be excessive, and there was little concern for mutagenicity of vinclozolin.

3. Infants and Children

a) Developmental Toxicity

Rat - From the oral developmental toxicity study in rats (Gray et al., 1993), the developmental NOEL was 3 mg/kg/day and the LOEL was 6.0 mg/kg/day based on the occurrence of pseudohermaphroditism (reduced anogenital distance) in male fetuses and nipple development. The maternal toxicity NOEL/LOEL were also 3 and 6 mg/kg/day, respectively, in this study and were based on reduced sex organ weights.

Rabbit - From the developmental toxicity study in rabbits (MRID# 41709301 and 41530501), the maternal (systemic) NOEL was 50 mg/kg/day, based on increased absolute and relative liver weight, reduced defecation, and reddish-brown urine at the LOEL of 200 mg/kg/day. The developmental (fetal) NOEL was 200 mg/kg/day, based on early resorptions, fetal weight increase, decrease live litter size and possible increased skeletal anomalies at the LEL of 400 mg/kg/day.

b) Reproductive Toxicity

Rat - From the reproductive toxicity study in rats (MRID# 42581301 and 42581302), the parental (systemic) NOEL was 4.9 mg/kg/day, based on decreased epididymal weights at the LOEL of 30 mg/kg/day. The reproductive/developmental (pup) NOEL was 4.9 mg/kg/day, based on reduced epididymal weights and lenticular degeneration at the LEL of 30 mg/kg/day.

Occupational Exposure

1. According to the proposed label (Ronilan DF, EPA Reg. No. 7969-85), applicators and other handlers must wear: coveralls over long-sleeved shirt and long pants, waterproof gloves, chemical-resistant footwear plus socks, protective eyewear, chemical-resistant headgear for overhead exposure, chemical-resistant apron when cleaning equipment, mixing, or loading, and a respirator (dust/mist outdoors, organic vapor enclosed

areas). This work clothing and personal protective equipment (PPE) exceeds the requirements (based on acute toxicity of the formulation) of the Worker Protection Standard (WPS).

2. Acute data for the technical are available. Based on these data, the 12-hour Restricted Entry Interval (REI) appearing on the label is in compliance with WPS. However, HED is currently working on the vinclozolin Reregistration Eligibility Document (RED). This review has resulted in a significant increase of the current REI from 12-hours to 10 days. This REI was based on a intermediate-term NOEL of 1.2 mg/kg. The TESC recently changed the short- and intermediate-term endpoint to 3 mg/kg. As a result, using the same assumptions as in the original calculations (transfer coefficient 1000 cm^2/hr), on DAT 0, 1, 2, and 3, the MOEs are 73, 84, 98, and 110, respectively (Table 7). Since the original study on strawberries was based on an application rate of 1.0 lb ai/A and the current snap bean rate is 0.5 lb ai/A, these estimated MOEs could be conservative.

However, in a review dated May 29,1996 (J. Leahy/OREB to K. Boyle/RCAB, attached), OREB responded to the issue of the two rates which was raised by BASF following completion of the Draft HED Chapter of the Vinclozolin RED. OREBs response stated "If the application rate for snap beans is less than 1 lb ai/acre, OREB agrees that the FDRs will likely be lower also. ..... OREB notes, however, that such a **linear relationship between application rate and FDRs has not been demonstrated and should not be assumed.**" In this memo, OREB recommended that if snap bean Section 18s were to continue or if a Section 3 registration was to be considered, the registrant should be required to submit a foliar dislodgeable residue (FDR) study for snap beans [132-1(a)].

PIRAT believes, taking into consideration the 0.5 lb ai/A application rate and the use of the 1000 cm^2/hr TC, that a 3 day REI should be established until FDR data are provided by the registrant. Submission of the required study, could result in a modification of the REI.

3. Occupational exposure assumptions and estimates of exposure are summarized in Tables 8 and 9, respectively. PIRAT has conducted its estimate of exposure with mixer/loaders and groundboom applicators wearing two layers of clothing, gloves and a dust/mist respirator. Currently, data in the Pesticide Handlers Exposure Database (PHED) are only available for a single layer of clothing plus gloves. The protection factor resulting from a second layer of clothing and dust/mist respirator have been arithmetically estimated assuming an exposure reduction factor of 50% and 80%, respectively.

Currently, PHED does not contain sufficient data entries to

quantify the degree of protection provided by protective eyewear and a chemical-resistant apron. Additionally, current OREB policy prohibits a second arithmetic correction to estimate dermal protection factors. Consequently, estimates of exposure may be conservative. **However, without additional data, PIRAT can not refine its estimate of exposure for mixer/loaders.**

Calculations for aerial applicators assume a single layer of clothing. Pilots operating aircraft with enclosed cockpits are not required to wear coveralls, respirator, or gloves.

For aerial application, the label states "When applying Ronilan DF by air, use **less than** (emphasis added) 20 gallons of spray solution per acre". On April 17, 1997, J. Leahy/OREB was contacted by A. Tobia/BASF and informed that the minimum spray solution for aerial application would be **no less than 5 gal/A.** PIRAT has based its estimates of the acreage treated by air during a 3 hour period on a final spray solution of 5 gal/A. PIRAT has estimated that 351 acres could be treated with this spray solution. More favorable flying conditions would result in more acres treated on a daily basis.

RD should insure that the Ronilan DF label is corrected and contains the minimum aerial spray solution of 5 gal/A.

4. HED has calculated short and intermediate - term MOEs of 500 for ground mixer/loaders and 1900 for ground applicators. MOEs for workers utilizing aerial equipment are 91 for mixer/loaders and 700 for pilots. In the best scientific judgement of PIRAT, these MOEs do not exceed HED's level of concern for occupationally exposed workers.

Dietary Exposure

1. The nature of the residue in plants is adequately understood based on metabolism studies on strawberries, lettuce, and peaches (see Chemistry Chapter of the RED, memo of S. Knizner dated 10/4/95). The residue of concern is vinclozolin and its metabolites containing the 3,5-dichloroaniline (DCA) moiety, as specified in 40 CFR 180.380.

2. The nature of the residue in animals is adequately understood based on ruminant and poultry metabolism studies (see Chemistry Chapter of the RED, memo of S. Knizner dated 10/4/95). The residue of concern is vinclozolin, a mixture of the diastereomers of N-(3,5-dichlorophenyl)-2-methyl-2,3,4-trihydroxybutyramide (BF 352-25), and a mixture of diastereomers derived by dihyroxylation of the vinclozolin vinyl group (BF 352-37). These metabolites are covered by the present tolerance expression, as specified in 40 CFR 180.380.

3. Adequate analytical methodology is available for data collection and enforcing tolerances of vinclozolin *per se* and its metabolites containing the 3,5-DCA moiety in/on plant commodities. Method I in PAM, Vol. II, a GC/ECD method, underwent a successful EPA method validation on strawberries. The limit of quantitation is 0.05 ppm.

As noted in the Chemistry Chapter of the RED (see memo of S. Knizner dated 10/4/95), data from analysis of residues of vinclozolin and its 3,5-DCA-containing metabolites in plants have been collected using BASF Methods 25, 25D, and 25F, which are comparable to Method I in PAM, Vol. II.

The FDA PESTDATA database dated 1/94 (Pam Vol. I, Appendix II) indicates that vinclozolin is completely recovered (>80%) using FDA Multiresidue Protocols D and E (oily and non-oily matrices). Vinclozolin metabolite B is completely recovered using Protocols D and E (for oily matrices) and only partially recovered (50-80%) using Protocol E for non-oily matrices. Metabolite E is completely recovered using Protocol D. Metabolite F is recovered using Protocol D but no quantitative information is available. Metabolite S is partially recovered using Protocol E (non oily matrices). The FDA multiresidue methodology differentiates between vinclozolin and iprodione, a pesticide which also contains a DCA moiety.

4. As noted in the Chemistry Chapter of the RED (see memo of S. Knizner dated 10/4/95), the requirements for storage stability data have been satisfied for purposes of reregistration. In general, vinclozolin residues in plants are stable for 17-40 months under frozen conditions. Storage stability data submitted in conjunction with petition PP#9F3750 indicated that vinclozolin residues are stable in animal matrices for up to 2 years at -20 C. For pending petitions, acceptable storage stability studies have been conducted using fortified control samples of succulent beans (PP#9F3762/FAP#9H5585) and potatoes (PP#1F4008/FAP#2H5623). These data indicate that residues of vinclozolin *per se* are stable in frozen succulent beans for up to 68 days and in potatoes for up to 6 months.

5. Residues of vinclozolin and its metabolites containing the 3,5-dichloroaniline (DCA) moiety are not expected to exceed 2.0 ppm in/on snap beans as a result of this Section 3 registration. **The registrant should submit a revised Section F requesting the establishment of a tolerance for regulable vinclozolin residues in/on snap beans at 2.0 ppm.**

6. No processed commodities are associated with snap beans (Table 1 of OPPTS 860.1000, 7/31/96).

7. No feed items are associated with snap beans (Table 1 of OPPTS 860.1000, 7/31/96). Therefore, secondary residues are not

expected as a result of this proposed Section 3 registration.

8. As noted in the Chemistry Chapter of the RED (see memo of S. Knizner dated 10/4/95), the EFED Phase 4 Review (A.Jones, 3/25/91) required a confined rotational crop study and reserved data requirements for a field rotational crop study. The EFED Phase 4 Environmental Fate Summary Table for Vinclozolin (A. Jones, 3/20/91) noted that MRID #41496905 (dated January, 1984) was not cited in the registrants Phase 3 Response, although it was summarized in the summary for the confined rotational crops (MRID #9219030). EFED concluded that MRID #41496905 should be reviewed in Phase 5.

MRID #41496905 has been reviewed and was found to be inadequate and not upgradeable (CBRS No. 16222, DP Barcode D219494, 9/25/95, S.Knizner). The registrant should conduct a new study to fulfill Guideline 165-1 data requirements. Guidance concerning confined rotational crop studies can be found in the guidance document entitled "Follow Up Guidance for Conducting Rotational Crop Studies", E.Zager and D.Edwards, 2/23/93, EPA 738-B-93-001, February 1993.

EFED has previously established rotation intervals in conjunction with review of data submitted in MRID #00136385 (3/25/80). The intervals established should be used until acceptable confined and/or field rotational crop studies are submitted. The requirement for a new confined rotational crop study will not impede making the reregistration eligibility decision for vinclozolin.

The following recommendations concerning rotational crops were made in the memo of E.A. Resek dated 3/20/91 (EFGWB memo concerning MRID# 00136385):

> Rotational crop data permits rotation only to the following and only when indicated total pounds active ingredient applied per acre have not been exceeded through the previous season:
>
> Lettuce may be planted 6 months after treatment, not exceeding 12 lbs.ai./A.
> Squash may be planted 2 months after treatment, not exceeding 9 lbs.ai./A.
> Corn may be planted 2 months after treatment, not exceeding 9 lbs.ai./A., with use of only the corn grain for food and/or feed purposes.
> Spring wheat may be planted 9 months after treatment, not exceeding 8 lbs.ai./A.

Data requirements for a field rotational crop study are reserved pending receipt of an adequate confined rotational crop study. **In the interim, the proposed label should be changed to limit rotation within 12 months to crops which have**

tolerances with U.S. Registrations. Based on the RECOMMENDATIONS section of this memo, this would allow unrestricted rotation to the following non-tree crops: caneberries, garlic, onions, lettuce, shallots, and strawberries. All other crops should be restricted to a 12-month rotational crop interval.

9. A CODEX MRL for residues of vinclozolin and its metabolites containing the 3,5-dichloroaniline moiety has been established for common beans at 2.0 ppm. Residue data were examined at the Joint meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues, Rome, 9/29-10/8/86. The field trials were conducted in Germany, the Netherlands, Japan, United Kingdom, and France. At the meeting, it was decided that a 2.0 ppm MRL should be established based on rates of 0.19 (3 applications) to 1.0 kg.ai./ha. (3 applications) and a PHI of 7 days. These rates are equivalent to 0.17 to 0.89 lbs.ai./A.

10. Acute Dietary Risk. For acute dietary risk assessment, the TES Committee recommended the use of the NOEL of 5.5 mg/kg/day in a developmental toxicity study in rats (Gray et al., 1993) for evaluating acute risks to females 13+ years, based on developmental findings.

As noted in the memo of K. Boyle signed 8/9/96, in response to the acute dietary assessment performed by HED (Tier 1 modeling as outlined in "Final Office Policy for Performing Acute Dietary Exposure Assessment, D. Edwards, 6/13/96) and documented in the HED Chapter of the Vinclozolin RED (memo of K. Boyle signed 4/8/96), BASF submitted "Acute Dietary Exposure: Vinclozolin" (document dated 3/29/96 - MRID# 439835-01), BASF's consultant TAS (Technical Assessment Systems, Inc.) performed an acute dietary assessment using TAS EXPOSURE 4 software with the Monte Carlo option (Tier 3 modeling as outlined in "Final Office Policy for Performing Acute Dietary Exposure Assessment, D. Edwards, 6/13/96). TAS's acute dietary assessment was performed using the acute anticipated residues outlined in the memo of S.Knizner dated 11/15/95, along with percent crop treated (supplied by BEAD) and percent imported data (supplied by USDA) that were used in the HED RED Chapter. The results of the TAS analysis resulted in an MOE = 90 at the 99.9th percentile (exposure = 0.0608848 mg/kg/day).

The Monte Carlo analysis used in TAS's 3/29/96 run used discrete distribution in their Monte Carlo modeling. Rather than using a range of field trial residue data which reflected the current labeled use pattern and PHI, the run incorporated only two possibilities of residue values - either residues were at the highest field trial level (as outlined in the memo of S. Knizner dated 11/15/95) or they were zero (reflecting

the percentage of the crop which would not have been treated or percentage of the crop which would not have been imported for crops which have tolerances but no U.S. registrations). A more realistic and refined calculation of dietary exposure would include Monte Carlo modeling using the entire distribution of residue data which reflect the current labeled use pattern and PHI. This approach was recommended by the National Research Council in their publication Pesticides in the Diets of Infants and Children, National Academy Press, 1993.

In the most recent acute dietary assessment, TAS submitted an updated version of "Acute Dietary Exposure: Vinclozolin" (document dated 3/29/96 - MRID# 439835-01), which received a new completed date of 4/28/97 and a new MRID# 442627-01. This assessment differed from the 3/29/96 assessment in that it used the entire range of field trial residue data which reflected the current labeled use pattern and PHI for single-serving commodities for which vinclozolin has a U.S. registration (apricots, caneberries, cherries, cranberries, garlic, lettuce (leaf and head), nectarines, onions, peaches, shallots, snap beans, and strawberries). For the sole blended commodity, imported wine grapes, TAS used the high-end residue value from monitoring data from USDA's Pesticide Data Program (PDP). Of the 587 imported grape samples analyzed by PDP, 165 samples contained detectable vinclozolin residues, up to 0.88 ppm. The high-end residue value of 0.88 was assumed for fresh/whole grapes, and was multiplied by the default processing factor of 1.0 to represent wine and sherry. For commodities without a U.S. registration ("import" tolerance - cucumbers, Belgian endive, kiwifruit, and bell peppers), PIRAT (in consultation with the DRES Section Head and two Chemistry Branch Senior Scientists) recommended that TAS use single residue values which represented the highest field trial level at the currently labeled (foreign) use rates and PHIs. PIRAT believes that, since the Agency has no control over the foreign uses, and there is no mechanism for the Agency to be informed of changes in foreign vinclozolin labels if they were to occur, a more conservative approach needs to be taken (similar to the 3/26/96 TAS run), rather than using the entire range of foreign field trial residue values.

In examining the raw data field trial data submitted in the Monte Carlo analysis by TAS and the memos of S. Knizner dated 10/4/95 and 11/15/95, it appears that much of the raw data that was submitted to TAS by BASF was not available or able to be accessed for review with the RED. In some cases, the high-end field trial data recommended by PIRAT to be used for the "imported" commodities differed from those recommended for use in the HED Chapter of the Vinclozolin RED (see memo of S. Knizner dated 11/15/95). The values recommended by PIRAT

and the CBRS memo of 11/15/95 are harmonious with respect to the following crops: Belgian endive (1.4 ppm), kiwifruit (8.4 ppm), and peppers, bell (1.09 ppm). However for cucumbers, PIRAT recommended 1.0 ppm and CBRS 0.27 ppm. The data that are the basis of this recommendation were not available or able to be accessed by CBRS for review with the RED.

Differences in residue levels reflecting domestic uses were also present. In some cases, PIRAT recommended that residue values be used in the Monte Carlo analysis which are higher than the tolerance. This occurred with the following crops: leaf lettuce, onions (dry bulb), and snapbeans. Residue data examined were all below tolerances for the following crops: caneberries, cherries, cranberries, head lettuce, apricot, nectarines, peaches, and strawberries. A detailed discussion of residue levels used for these commodities follows

Leaf Lettuce

In the case of leaf lettuce, there was a group of 6 samples (sample codes RCN 5033-3 through RCN 5033-5) that were apparently conducted properly in regards to the label use directions, but exhibited much higher residues (ranging from 10.00 ppm to 17.60 ppm - the current tolerance is 10 ppm). These data were apparently not available/able to be accessed for review with the RED. PIRAT requested additional information on the field trials from TAS/BASF. PIRAT received the following additional information concerning the trials:

- the trials were conducted in CA in 1985 by IR-4
- the crop was harvested 53 days after planting (for 28-day PHI samples)
- in the field report, the following denotation was made: "sample size small"

BASF stated that the crop was planted later than normal (11/3/85) and was stunted at harvest. BASF stated that the typical maturity for a winter crop of lettuce would be 120 days and a summer crop would be 90 days. However, in consultation with B. Schneider (CBTS) and available reference data, PIRAT arrived at a typical summer harvest time for leaf lettuce at 45 days. Therefore, PIRAT does not believe that the 53-day harvest time is atypical. Concerning the fact that the harvested leaf lettuce was deemed to exhibit a small sample size, PIRAT believes that, due to growing season variation from year-to-year, this situation would be encountered. While the lettuce size might not be "typical" or "average", it still may be marketable. PIRAT notes that FDA has reported finding incidents of finding over-tolerance residues of acephate on head lettuce, where the growing conditions favored development of small heads. These heads had been harvested and were destined for supermarkets. For

use in a chronic risk assessment, use of the samples may not be appropriate without averaging or weighting the data, but for use in acute risk assessment, PIRAT believes that it is appropriate to use the data from these field trials.

For these reasons, PIRAT recommended that the residues be used as part of the Monte Carlo acute analysis. PIRAT does not believe that this decision necessitates an increase in the current 10.0 ppm tolerance, however, this decision should be made in conjunction with the RED.

Onions

In the case of onions, CBRS examined the over-tolerance data from field trials in California (trial# 17490) and recommended that the current tolerance be raised from 1 ppm to 6 ppm. However, it appears that the field trial data from the CAR 129-89 site were not available/able to be accessed for review with the RED. These field trials exhibit residues up to 8.40 ppm from field trials which match the proposed label rate and PHI. For this reason, PIRAT recommended that the residues be used as part of the Monte Carlo acute analysis. PIRAT does not believe that this decision necessitates an increase in the 6.0 ppm tolerance proposed in the HED Chapter of the RED, however, this decision should be made in conjunction with the RED.

Snap Beans

In the case of snap beans, several field trial samples exhibited residues above the 2 ppm tolerance that PIRAT is recommending for. The field trial residue studies conducted in California exhibit higher residues (up to 2.4 ppm) than those from other states (NY - up to 0.76 ppm; NC - up to 0.67 ppm; FL - up to 0.53 ppm; MI - up to 0.73 ppm; and OR - up to 0.95 ppm). This may be due to the decreased rainfall in CA, coupled with the extensive use of ground irrigation (rather than overhead irrigation). California has never requested or been granted a Section 18 for use of vinclozolin on snap beans. Requests have been received from the following states: MI, MN, NY, OR, PA, WA, and WI (private conversation with Libby Pemberton, ERMUS/RD/OPP).

A CODEX MRL for residues of vinclozolin and its metabolites containing the 3,5-dichloroaniline moiety has been established for common beans at 2.0 ppm. Residue data were examined at the Joint meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues, Rome, 9/29-10/8/86. The field trials were conducted in Germany, the Netherlands, Japan, United Kingdom, and France. At the meeting, it was decided that a 2.0 ppm MRL should be established based on

rates of 0.19 (3 applications) to 1.0 kg.ai./ha. (3 applications) and a PHI of 7 days. These rates are equivalent to 0.17 to 0.89 lbs.ai./A.

In light of harmonizing with CODEX, detailed examining the CODEX field trial data (including application rates and PHIs), and examining the U.S. data where vinclozolin will be used (including application rates and PHIs), PIRAT believes that a 2.0 ppm tolerance is appropriate for domestic snap beans. However, since none of the field trial residue data mimic that of the proposed use - the field trial rates were all double the proposed use (1.0 lb.ai./A./application vs. 0.5) and the PHIs were longer (typically 14 days in the field trials versus the proposed PHI of 9 days), PIRAT recommended that all of the available residue data be used in the acute Monte Carlo analysis.

Summary

The percent crop treated and percent imported data that were used to assign "zeros" to the residue data in the Monte Carlo runs were the same values used in the HED Chapter of the RED. As was done with the DRES chronic run, for commodities for which no percent crop-treated data were provided (blackberries, boysenberries, dewberries, loganberries, cranberries, garlic), a default of 100% was used, and for commodities for which no percent crop-imported data were provided (kiwi, chicory, Belgian endive, and wine/sherry), a default of 100% was used. In the TAS Monte Carlo Analysis (MRID# 442627-01), the residue values which are marked with a "*" were the values used in the Monte Carlo run.

The results of the Tier 3 analysis conducted with 1,000 iterations resulted in the 99.9th percentile exposure of 0.013587 mg/kg/day and an MOE of 405 (at the 99.9th percentile) for women of childbearing age (females 13+ years).

11. Chronic Dietary Risk.

The chronic dietary (food only) risk assessment used percent of crop treated/percent imported data to refine the risk estimate for selected commodities (apricots, beans, raspberries, cherries, cucumbers, lettuce, nectarines, onions, peaches, peppers, and strawberries.), while other commodities were assumed to be 100% treated/imported (caneberries (other than raspberries), cranberries, endive, garlic, wine/sherry, kiwifruit, and shallots). No chronic anticipated refinement has been performed. Therefore, the resulting exposure (food only) estimates should be viewed as partially refined; further refinement using anticipated residues and additional percent of crop treated/percent imported data would result in lower chronic dietary exposure estimates. The tolerance values

outlined under the **RECOMMENDATION** section of this memo (along with the Assumptions listed below) result in an Anticipated Residue Contribution (ARC) that is equivalent to the following percentages of the RfD:

Subpopulation	ARC_{food} Value (mg/kg/day)	% RfD
U.S. Population	0.001383	12%
Nursing Infants	**0.000867**	**7%**
Non-Nursing Infants (<1 year old)	**0.001679**	**14%**
Children (1-6 years old)	**0.001455**	**12%**
Children (7-12 years old)	**0.001075**	**9%**
U.S. Population (Spring Season)	0.001622	14%
Northeast Region	0.001695	14%
Western Region	0.001822	15%
Females 13+ Years, Nursing	0.001645	14%
Females (20 Years and Older, Not Pregnant or Nursing)	0.001526	13%

The subgroups listed above are: (1) the U.S. population (48 states); (2) those for infants and children; and, (3) the other subgroups for which the percentage of the RfD occupied is greater than that occupied by the subgroup U.S. population (48 states).

In addition to the changes recommended in the **RECOMMENDATIONS** section of this memo, the following assumptions were made in the chronic DRES analysis:

- no anticipated residue refinement was performed
- the same percent crop-treated data were used in the DRES analysis that were provided by BEAD (data from 1992 to 1994) for use in the HED Chapter of the RED (memo of K. Boyle signed 4/8/96)
- for commodities for which no percent crop-treated data were provided (blackberries, boysenberries, dewberries, loganberries, cranberries, garlic, and shallots), a default of 100% was used.
- the same percent import data were used in the DRES analysis that were provided by BEAD (data from 1990 to 1993) for use in the 4/8/96 memo.
- for commodities for which no percent crop-imported data were provided (kiwi, chicory, Belgian endive, and wine/sherry), a default of 100% was used.

12. Dietary Cancer Risk.

The Cancer Peer Review Committee (CPRC) met on 1/15/97 (3rd Meeting, memo dated 4/3/97) to re-evaluate the carcinogenic potential of vinclozolin, based on revised pathology results. The majority of the CPRC agreed that vinclozolin should be classified as Group C chemical - possible human carcinogen, with a non-linear approach (MOE)

based on a NOEL of 4.9 mg/kg/day for hormone-related effects (decreased epididymal weight at 30 mg/kg/day) in the 2-generation oral reproductive toxicity study in rats to quantify human risk. The MOE approach was chosen because the remaining tumors (Leydig cell) were benign at dose levels which were not considered to be excessive, and there was little concern for mutagenicity of vinclozolin.

The Anticipated Residue Contribution (ARC) from the chronic DRES analysis for the U.S. Population was calculated to be 0.001383 mg/kg/day. Using the formula where the Margin of Exposure (MOE) = NOEL (mg/kg/day) ÷ Exposure (mg/kg/day), or 4.9 mg/kg/day ÷ 0.001383 mg/kg/day, the calculated MOE (food only) is 3,500.

Exposure from Water

The following information was noted in the Environmental Fate and Ground Water Branch (EFGWB) memo of H.M. Jacoby dated 8/1/95 concerning vinclozolin as a List B RED candidate:

> "Acceptable and supplemental laboratory and field data indicate that parent vinclozolin is relatively labile and dissipates in the environment by microbial-mediated hydrolysis (soil metabolism), abiotic degradation, and transport with water. N-(3,5-dichlorophenyl) carbamic acid (1-carboxyl-1-methyl)-2-propenyl ester (metabolite B or BF 352-22) is a common degradate of hydrolysis, soil metabolism, and photolysis. Because metabolite B is formed rapidly and in relatively large concentrations at environmental pH, it may have biological activity and contribute to the pesticidal properties of parent vinclozolin. The other principal degradation products of vinclozolin are 3,5-dichloroaniline (metabolite D or BF 352-31); and N-(3,5-dichlorophenyl)-2-hydroxy-2-methyl-3-butenoic acid amide (metabolite E or BF352-23). Other degradates are formed in smaller concentrations. Metabolite E, which appears to be a degradation product of parent and metabolite B, degrades to 3,5-dichloroaniline (metabolite D) which appears to resist further degradation. Metabolites B, D, and E are potentially very mobile to slightly mobile and may be transported with water through the soil profile or with surface runoff. Residues are likely to be most mobile in sandy soils low in organic matter."

Surface Water

In a memo dated 2/27/97 from R.D. Jones (RCAB), Tier 1 Estimated Environmental Concentrations (EEC's) were calculated with GENEEC for use in human health risk assessments for vinclozolin (see Attachment III). The calculated acute EEC is 27.04 µg/L and

the calculated chronic EEC is 1.06 µg/L. The model was performed using residues of vinclozolin per se. However, due to the very conservative nature of the Tier 1 GENEEC run and low estimated metabolite level in relation to the parent compound, this estimate should be applicable to the sum total of vinclozolin and its metabolites containing the 3,5-dichloroaniline moiety (private conversation with R.D. Jones on 3/18/97).

Exposure

Adult Females (13+ years)

Exposure = (chemical concentration in µg/L in consumed water) X (10^{-3} mg/µg) ÷ (60 kg body weight) X (2L water consumed/day)

for acute, Exposure = (27.04 µg/L) X (10^{-3} mg/µg) ÷ (60 kg body weight) X (2L/day)
= 0.000901 mg/kg/day
for chronic, Exposure = (1.06 µg/L) X (10^{-3} mg/µg) ÷ (60 kg body weight) X (2L/day)
= 0.0000353 mg/kg/day

Other Adult Subgroups

Exposure = (chemical concentration in µg/L in consumed water) X (10^{-3} mg/µg) ÷ (70 kg body weight) X (2L water consumed/day)

for acute, Exposure = (27.04 µg/L) X (10^{-3} mg/µg) ÷ (70 kg body weight) X (2L/day)
= 0.0007726 mg/kg/day
for chronic, Exposure = (1.06 µg/L) X (10^{-3} mg/µg) ÷ (70 kg body weight) X (2L/day)
= 0.0000303 mg/kg/day

Child

Exposure = (chemical concentration in µg/L in consumed water) X (10^{-3} mg/µg) ÷ (10 kg body weight) X (1L water consumed/day)

for acute, Exposure = (27.04 µg/L) X (10^{-3} mg/µg) ÷ (10 kg body weight) X (1L/day)
= 0.00270 mg/kg/day
for chronic, Exposure = (1.06 µg/L) X (10^{-3} mg/µg) ÷ (10 kg body weight) X (1L/day)
= 0.000106 mg/kg/day

Risk

Margin of Exposure (MOE) = NOEL (mg/kg/day) ÷ Exposure (mg/kg/day)
%RfD = Exposure (mg/kg/day) ÷ RfD (mg/kg/day) X 100%

Acute

for females 13+ years (only subgroup of concern)
MOE = (5.5 mg/kg/day) ÷ (0.0009013 mg/kg/day)
= 6,100

Chronic

Using a value of 0.012 mg/kg/day for the RfD, the following risks were calculated:

Subpopulation	Exposure (mg/kg/day)	% RfD
U.S. Population	0.0000303	< 1%
Nursing Infants	**0.000106**	**< 1%**
Non-Nursing Infants (<1 year old)	**0.000106**	**< 1%**
Children (1-6 years old)	**0.000106**	**< 1%**
Children (7-12 years old)	**0.000106**	**< 1%**
U.S. Population (Spring Season)	0.0000303	< 1%
Northeast Region	0.0000303	< 1%
Western Region	0.0000303	< 1%
Females 13+ Years, Nursing	0.0000353	< 1%
Females (20 Years and Older, Not Pregnant or Nursing)	0.0000353	< 1%

Cancer

For the U.S. Population, an MOE (dietary water only) of 160,000 was calculated from the exposure value of 0.0000303 mg/kg/day.

Ground Water

Based on current EFED data, the parent vinclozolin molecule is not likely to be persistent in the environment (private conversation with R.D. Jones, 4/3/97). However, degredates of vinclozolin are mobile and can be persistent under certain environmental condition. At the current time, the potential levels of vinclozolin metabolites in ground water cannot accurately be assessed. The ground water issue will be addressed in the HED Chapter of the Vinclozolin RED.

Non-Dietary Non-occupational Exposure

According to a search of the Reference File Systems (REFS) on 04/29/97, vinclozolin is currently registered for use on the following residential non-food sites: ornamental flowering plants

(2 products; EPA Reg. Nos. 7969-85 and 58185-17) and ornamental turf (4 products; EPA Reg. Nos. 7969-53, 62, 85, and 58185-17).

The Agency has residential-related exposure data (turf) to complete a risk assessment for vinclozolin. Based on these data, postapplication exposure to adults and toddlers from vinclozolin treated turf, in the best scientific judgement of PIRAT, would pose a risk that exceeds HED's level of concern. Currently, no data are available to estimate residential exposure from the use of vinclozolin on ornamental flowering plants.

OREB has determined that the following four scenarios[8] are the likely worst-cases for residential exposures to vinclozolin, based on labeled uses of vinclozolin:

1. Homeowner handler exposure-- Mixing/loading/applying vinclozolin to home lawns or gardens with low pressure handwand sprayer (dermal and inhalation exposure).

2. Postapplication exposure to vinclozolin-treated turf (lawns).
   (a) Adult and toddler dermal exposure.
   (b) Toddler oral exposure.

3. Postapplication dermal exposure to vinclozolin-treated home gardens.
   (a) Adult harvesting garden or orchard produce such as peaches, beans, etc.
   (b) Child (age 10 - 12 yrs) harvesting garden or orchard produce.

4. Postapplication exposure to vinclozolin-treated produce at "U-pick" farms.
   (a) Adult harvesting strawberries or peaches.
   (b) Child harvesting strawberries or peaches.

   * Note that individuals harvesting "U-pick" are also likely to eat the treated produce as they harvest, resulting in dietary exposure in addition to the dermal exposures estimated here.

General assumptions and data sources:

- Body weights: Adult body weight is assumed to be 60 kg (endpoint based on developmental/maternal toxicity); toddlers are assumed to weigh 15 kg (3 yrs old); children 10 yrs old assumed to weigh 35 kg.[9]

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[8] Information pertaining to residential exposure scenarios was provided by John Leahy, OREB/HED.

[9] U.S. EPA (1996) Exposure Factors Handbook [Draft].

- Endpoints for risk assessment: Adult Female NOEL = 3 mg/kg/day for both short-term and intermediate-term exposures.[10] Child NOEL = 5 mg/kg/day for short-term exposure.[11]

- Dermal absorption = 25%

- Handler exposure data: PHED V1.1.

- Postapplication exposure data: Several vinclozolin-specific studies have been submitted by the registrant; these are referenced by MRID number for each scenario below where the data have been applied; where appropriate chemical specific data are not available, OREB has used best estimates in lieu of actual data.

SCENARIO 1. Homeowner Handler Exposure: Mixing/loading/applying vinclozolin to home lawns or gardens with low pressure handwand equipment.

Daily dermal exposure is calculated using the following formula:

Daily dermal exposure (mg/day) = Unit exposure from PHED (mg/lb ai) * application rate (lb ai/gal) * gallons handled (gal/day)
Where Dermal unit exposure value = 103 mg/lb ai (PHED V1.1),
Application rate = 0.0075 lb ai/gallon of spray solution, and
Amount handled = 5 gallons of spray solution per day for homeowners.

Daily dermal exposure = 3.9 mg/day.

Daily inhalation exposure is calculated using the following formula:

Daily inhalation exposure (mg/day) = Unit exposure (ug/lb ai) * application rate (lb ai/gal) * gallons handled (gal/day) * conversion (1 mg/1,000 ug)

Where: Inhalation unit exposure = 31 ug/lb ai (PHED V1.1),
Application rate = 0.0075 lb ai/gallon of spray solution, and
Amount handled = 5 gallons of spray solution per day for homeowners.

Daily inhalation exposure = 0.001 mg/day.

Daily total exposure (dermal + inhalation exposure) = 3.9 mg/day.

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[10] U.S. EPA (1996) Toxicology Endpoint Selection Committee Document, dated 7/18/96.

[11] U.S. EPA (1997) Memorandum from D. Anderson/TB-I to K. Boyle/RCAB dated 4/30/97.

DOSE AND RISK

Dose (absorbed) is calculated using the following formula:

Dose (mg/kg/day) = Exposure (mg/day) * absorption (25% dermal, 100% inhalation) / body weight (bw)

Dermal dose = 0.016 mg/kg/day
Inhalation dose = 0.00002 mg/kg/day

Total Dose = 0.016 mg/kg/day

Risk, in terms of margin of exposure (MOE), is calculated using the following formula:

MOE = NOEL (mg/kg/day) / Dose (mg/kg/day)

MOE = 188

Uncertainties Surrounding Scenario 1

The exposure data for this scenario come from PHED which is designed to represent occupational handlers' potential exposures. Therefore, these data may underestimate the exposure to a homeowner who is likely to be less skilled in pesticide mixing, loading, and application methods, have access to less sophisticated equipment, and be less knowledgeable about general safe practices for handling pesticides.

The assumption of 5 gallons of spray solution handled per day is believed to be an upper bound estimate; most homeowners would be likely to handle less spray solution per day.

Homeowners who treat the produce in their home gardens and orchards also harvest and eat the produce, resulting in additional dermal and dietary exposure which has not been factored into the risks estimated here.

SCENARIO 2. Postapplication Exposure to Vinclozolin-Treated Turf (Lawns).

Three dissipation and reentry studies were submitted for residential turf. The sites studied were in California, Florida, and Pennsylvania. The results of these studies are as follows:

Study 1: Dislodgeable Foliar Residue (DFR) of Vinclozolin (Ronilan® DF) in Turf, Florida Site. MRID No. 435287-01.

A dislodgeable foliar residue study of vinclozolin, formulated as Ronilan® DF, was conducted on turf in Florida. Four applications of Ronilan® DF were made to the turf at a rate of 5.6 lb ai/A. DFR

data were collected using two different methodologies: dislodging solution and cotton cloth. At the Florida site, residues were measured up to DAT 14. The dislodging solution was used to calculate a reentry interval. Residues were measured at 3.75 ug/cm^2 at day-after-treatment (DAT) 0 (typically after sprays dry) and declined to less than the detection limit at DAT 14.

Study 2: DFR of Vinclozolin (Ronilan® DF) in Turf, California and Pennsylvania Sites. MRID No. 433437-01.

A dislodgeable foliar residue study of vinclozolin, formulated as Ronilan® DF, was conducted on turf in California and Pennsylvania. Four applications of Ronilan® DF were made to the turf at a rate of 5.6 lb ai/A. DFR residues were calculated using two different methodologies: dislodging solution and cotton cloth. At the California site, residues were measured up to DAT 63 (the last day tested). At the Pennsylvania site, residues were measured up to DAT 63 (the last day tested). The dislodging solution was used to calculate the reentry interval. At the California site, residues were measured at 10.6 ug/cm^2 at DAT 0 after the last application and declined to 0.00120 ug/cm^2 at DAT 63. At the Pennsylvania site, residues were measured at 24.5 ug/cm^2 at DAT 0 after the last application and declined to 0.00438 ug/cm^2 at DAT 63.

Study 3: Evaluation of Turf Reentry Exposure in California to a Broadcast Application of Ronilan® DF. MRID No. 433437-02.

A turf reentry study of vinclozolin, formulated as Ronilan® DF, was conducted on workers at the same California site used in Study 8 (MRID No. 433437-01). Four applications of Ronilan® DF were made to the turf at a rate of 5.6 lb ai/A. Dermal exposure was measured on Day 0 after the last application when ten workers re-entered a treated turf field and performed a "jazercise" routine. Two dermal exposure replicates were taken from each worker. Dermal exposure to the test subjects re-entering the treated turf averaged 90.6 mg of vinclozolin/hr.

Postapplication dermal exposure is calculated using the following formula:

Dermal exposure = DFR (ug/cm^2) * Transfer Coefficient (cm^2/hr) * Duration (4 hrs/day)/Unit Adjustment from ug to mg (1000 ug/mg)

Because restricted-entry intervals (REIs) are generally not feasible for residential sites such as home lawns, only DAT 0 DFRs are considered. DFR values for the California, Pennsylvania, and Florida sites at DAT 0 are 5.1285 ug/cm^2, 12.436 ug/cm^2, and 4.0217 ug/cm^2 respectively. The average DFR for the three sites is 7.1954 ug/cm^2 at DAT 0.

The transfer coefficient derived in Study 3 is 8,547 cm^2/hr. Note that the DFR values for the California site were significantly

lower than the average DFR values for the three sites combined. When the "best fit" DFR values for the three sites combined is used to calculate the transfer coefficient, the Tc = 17,666 cm^2/hr. Therefore, use of the Tc derived in Study 3 may underestimate exposure when DFRs are higher than those at the California site in Study 3.

The duration is estimated to be 4 hours per day (1-4 age group at 90th percentile plays outdoors for 210 minutes per day, U.S. EPA, 1996).

Thus, **dermal exposure = 246 mg/day.**

Adult Dose = 1.03 mg/kg/day
Toddler Dose = 4.1 mg/kg/day

Adult Female Dermal MOE = 2.9
Toddler Dermal MOE = 1.2

Uncertainties Surrounding Scenario 2a

The assumption of 4 hours of exposure per day to treated turf is believed to be conservative for both adults and children, however, in some areas, such as those with typically good weather, this may underestimate exposure to children who may exceed 4 hours of play on treated turf.

The assumption of a 15 kg body weight for toddlers may underestimate exposure to children weighing less than 15 kg and overestimate risks to children weighing more than 15 kg..

No adjustment has been made for the smaller surface area of a child than the individuals who participated in the study from which the exposure data were derived.

The transfer coefficient (Tc) used in this scenario is derived from exposure data collected at the California site only, where the DFR values were lower than the average DFR values for the three sites combined. Combining the best fit DFR values from the three sites with the exposure data collected at the California site yields a Tc of 17,666 cm^2/hr.

OREB currently has insufficient data to estimate toddlers' potential oral exposure resulting from incidental ingestion. This exposure could be significant for some children, particularly those who exhibit pica syndrome.

SCENARIO 2b. Toddler Oral Exposure (from incidental ingestion of soil).

Toddlers experience oral exposure following applications of vinclozolin to residential turf in a variety of ways including (1)

inadvertent hand-to-mouth transfer of vinclozolin residues, (2) ingestion of turfgrass bearing residues, and (3) incidental ingestion of soil from treated lawns bearing vinclozolin residues. HED recognizes that children will ingest residues associated with applications to lawn, but currently does not have sufficient data to quantify the exposure.

SCENARIO 3. Postapplication Dermal Exposure to Vinclozolin-Treated Home Gardens and Orchards: harvesting produce such as peaches, beans, strawberries, etc. (a) Adult harvesting; (b) Child age 10-12 yrs harvesting.

OREB has selected harvesting peaches as a reasonable worst-case scenario to represent homeowner postapplication exposure to vinclozolin-treated home gardens and orchards.

Three reentry studies for peach orchards have been submitted for vinclozolin: MRID Nos. 428300-01 (DFR study at California and Georgia sites), 428300-02 (harvester exposure study at California site), and 435059-01 (DFR study at Pennsylvania site). At each of the three sites, vinclozolin was applied at a rate of 1 lb ai per acre, which is representative of the maximum application rate for fruits and vegetables. Residues were sampled before applications, and at intervals from DAT 0 through DAT 63. For the purposes of estimating homeowner harvester exposure, the DFR values from DAT 0 for each of the 3 sites were averaged. Since REIs are not feasible for homeowner uses, only DAT 0 residues are considered.

A harvester reentry study of vinclozolin (formulated as Ronilan® DF 50 percent ai) was conducted at the California site, concurrently with the DFR study. Dermal samples using passive dosimetry were collected on both DAT 0 and DAT 7. The results indicate that the highest exposure occurred on DAT 0 (cited as "after application," presumably after sprays had dried). A concurrent DFR study (MRID No. 428300-01) was completed in the same orchard, and the DFR data were used to calculate the slope of decline for vinclozolin over time. Using the "Best Fit" DFR and the concurrent dermal exposure data, the average transfer coefficient for DAT 0 was calculated to be 4,393 cm^2/hr. Since REIs are not feasible for homeowner uses, only the DAT 0 transfer coefficient is considered for this review.

DAT 0 "best fit" DFR values for the three sites average 0.61 ug/cm^2.

DAT 0 Tc = 4,393 cm^2/hr.

Homeowners are assumed to have 2 hours of exposure per day while harvesting home garden or orchard produce.

Postapplication dermal exposure is calculated using the following formula:

Dermal exposure = DFR (ug/cm^2) * Transfer Coefficient (cm^2/hr) * Duration (2 hrs/day) / Unit Adjustment from ug to mg (1000 ug/mg)

Thus, **dermal exposure = 5.4 mg/day.**

Adult Dose = 0.023 mg/kg/day
Child (10 yrs) Dose = 0.039 mg/kg/day
Adult Female Dermal MOE = 130
Child Dermal MOE = 128

* Note that individuals harvesting produce in their home gardens and orchards are also likely to eat some of the treated produce they harvest resulting in dietary exposure in addition to the dermal exposures estimated here.

Uncertainties Surrounding Scenario 3

The exposure data used in Scenario 3 are drawn from studies of workers harvesting produce as wage earners. This may overestimate the exposure for homeowners who harvest produce from their own gardens and orchards for non-monetary purposes.

The 2 hours estimated for time spent picking treated produce is believed to be a reasonable estimate; some individuals with particularly large gardens or orchards may exceed this resulting in risks greater than those estimated here.

Individuals harvesting treated produce from home gardens and orchards are also likely to eat the produce resulting in additional dietary and dermal exposure that has not been factored into the risk estimated here.

SCENARIO 4. Postapplication Dermal Exposure to Vinclozolin-Treated "U-Pick" Strawberries and Peaches. (a) harvesting strawberries, adult and child (10 yrs); (b) harvesting peaches, adult and child.

* Note that individuals harvesting U-Pick produce are also likely to eat some of the treated produce they harvest resulting in dietary exposure in addition to the dermal exposures estimated here.

Strawberries

Two reentry studies for strawberries have been submitted for vinclozolin from which postapplication strawberry harvesting exposure can be estimated: MRID No. 430130-04 (DFR study at two California sites and one Michigan site), and MRID No. 430130-03 (harvester exposure study at one California site). At each site, vinclozolin was applied six times, seven days apart, at a rate of 1 lb ai per acre, which is representative of the maximum application rate for strawberries. Residues were sampled before applications, and at intervals from DAT 0 through DAT 63. For the

purposes of estimating harvester exposure at "U-pick" strawberry farms, the DFR values from DAT 0 for each of the 3 sites were averaged. Since REIs do not apply to non-employees, such as individuals harvesting at "U-pick" farms, only DAT 0 residues are considered. No preharvest interval (PHI) currently appli[redacted] to strawberries.

A harvester reentry study of vinclozolin (formulated as Ronilan® DF 50 percent ai) was conducted at the one of the California sites (Madera County), concurrently with the DFR study. Dermal samples using passive dosimetry were collected on both DAT 0 and DAT 2 after the last of the six applications. The results indicate that the highest exposure occurred on DAT 0 (cited as "after application," presumably after sprays had dried). The data from the concurrent DFR study were used to calculate the slope of decline for vinclozolin over time. Using the "Best Fit" DFR and the concurrent dermal exposure data, the average transfer coefficient for DAT 0 was calculated to be 932 cm^2/hr. Since REIs do not apply to non-employees, such as individuals harvesting at "U-pick" farms, only the DAT 0 transfer coefficients are considered for this review.

DAT 0 "best fit" DFR values for the three sites average 1.23 ug/cm^2.

DAT 0 Tc = 932 cm^2/hr.

Individuals harvesting strawberries at "U-pick" strawberry farms are assumed to have 4 hours of exposure per day.

Postapplication dermal exposure is calculated using the following formula:

Dermal exposure = DFR (ug/cm^2) * Transfer Coefficient (cm^2/hr) * Duration (4 hrs/day) / Unit Adjustment from ug to mg (1000 ug/mg)

Thus, **dermal exposure = 4.59 mg/day.**

Adult Dose = 0.019 mg/kg/day
Child (10 yrs) Dose = 0.033 mg/kg/day

Adult Female Dermal MOE = 158
Child Dermal MOE = 152

Peaches

DFRs and transfer coefficients are drawn from the peach studies referenced above. Exposure and risk estimates have been calculated for DAT 0 and DAT 2 when MOEs exceed 100 for both children and adults. However, it is OREB's understanding that a preharvest interval of 14 days exists for stone fruit including peaches. Based on available data OREB believes that dermal MOEs exceed 100

by DAT 14 when the PHI expires and individuals would be permitted to harvest peaches on U-pick farms.

DAT 0 "best fit" DFR values for the three sites average 0.61 ug/cm^2.
DAT 2 "best fit" DFR values for the three sites average 0.38 ug/cm^2.

DAT 0 Tc = 4,393 cm^2/hr.

Individuals harvesting peaches at "U-pick" peach farms are assumed to have 4 hours of exposure per day.

Postapplication dermal exposure is calculated using the following formula:

Dermal exposure = DFR (ug/cm^2) * Transfer Coefficient (cm^2/hr) * Duration (4 hrs/day) / Unit Adjustment from ug to mg (1000 ug/mg)

Thus, **DAT 0 dermal exposure = 10.72 mg/day; and DAT 2 dermal exposure = 6.76 mg/day.**

DAT 0: **Adult Dose = 0.045 mg/kg/day**
Child (10 yrs) Dose = 0.077 mg/kg/day

Adult Female Dermal MOE = 67
Child Dermal MOE = 65

DAT 2: **Adult dose = 0.028 mg/kg/day**
Child dose = 0.048 mg/kg/day

Adult Female MOE = 107
Child MOE = 104

Uncertainties Surrounding Scenario 4

The exposure data used in Scenario 4 are drawn from studies of workers harvesting produce as wage earners. This may overestimate the exposure for non-occupational harvesters picking produce at "U-pick" farms for non-monetary purposes.

The 4 hours estimated for time spent picking treated produce in Scenario 4 is believed to be a conservative estimate; some individuals, however, may exceed this resulting in risks greater than those estimated here.

Individuals harvesting treated produce at U-pick farms are also likely to eat some of the produce resulting in additional dietary exposure that has not been factored into the risk estimated here.

Total Aggregate Risk

Acute Aggregate Risk

The acute dietary (food only) risk assessment used Monte Carlo modeling and percent of crop treated/percent imported data for selected commodities (apricots, beans, raspberries, cherries, cucumbers, lettuce, nectarines, onions, peaches, peppers, and strawberries.), while other commodities were assumed to be 100% treated/imported (caneberries (other than raspberries), cranberries, endive, garlic, wine/sherry, kiwifruit, and shallots). For the subgroup of concern, females 13+ years, the resulting high-end (99.9th percentile) dietary (food only) exposure estimate of 0.013587 mg/kg/day, when added to the surface water exposure estimate of 0.0009013 mg/kg/day, results in a dietary (food + water) **MOE of 380.**

Short- and Intermediate-Term Aggregate Risk

Short- and intermediate-term aggregate risk takes into account exposure from chronic dietary food and water (considered to be a background exposure level) plus indoor and outdoor residential exposure. Based on an examination of REFS on 4/29/97, there are no currently registered indoor uses of vinclozolin (only outdoor).

Using the exposures outlined under **Chronic Dietary Risk** and **Exposure from Water** sections of this memo, along with the short-term NOELs of 3 mg/kg/day (for ages 13+) or 5 mg/kg/day (for infants and children 1 - 12 years of age), the following chronic dietary (food + water) MOEs are calculated in Table 1.

Table 1

Chronic Dietary MOEs

Subpopulation	ARC_{food} Value (mg/kg/day)	Water Exposure (mg/kg/day)	Total Dietary Exposure (mg/kg/day)	MOE
U.S. Population	0.001383	0.0000303	0.001413	2100
Nursing Infants	**0.000867**	**0.000106**	**0.000973**	**5100**
Non-Nursing Infants (<1 year old)	**0.001679**	**0.000106**	**0.00179**	**2800**
Children (1-6 years old)	**0.001455**	**0.000106**	**0.00156**	**3200**
Children (7-12 years old)	**0.001075**	**0.000106**	**0.00118**	**4200**
U.S. Population (Spring Season)	0.001622	0.0000303	0.00165	1800
Northeast Region	0.001695	0.0000303	0.00173	1700
Western Region	0.001822	0.0000303	0.00185	1600
Females 13+ Years, Nursing	0.001645	0.0000353	0.00168	1800
Females (20 Years and Older, Not Pregnant or Nursing)	0.001526	0.0000353	0.00156	1900

Based on the 4 scenarios outlined under the **Residential Exposure** section of this memo, MOEs for 5 combinations of food, water, and residential exposure were calculated as shown in Tables 2 through 6.

Table 2

Aggregate Risk from Chronic Dietary + Short-Term Homeowner Handler

Subpopulation	Chronic Dietary Exposure (mg/kg/day)	Homeowner Handler Exposure (mg/kg/day)	Total Exposure (mg/kg/day)	MOE
U.S. Population	0.001413	0.016	0.017413	170
Nursing Infants	**N/A**	**N/A**	**N/A**	**N/A**
Non-Nursing Infants (<1 year old)	**N/A**	**N/A**	**N/A**	**N/A**
Children (1-6 years old)	**N/A**	**N/A**	**N/A**	**N/A**
Children (7-12 years old)	**N/A**	**N/A**	**N/A**	**N/A**
U.S. Population (Spring Season)	0.00165	0.016	0.01765	170
Northeast Region	0.00173	0.016	0.01773	170
Western Region	0.00185	0.016	0.01785	170
Females 13+ Years, Nursing	0.00168	0.016	0.01768	170
Females (20 Years and Older, Not Pregnant or Nursing)	0.00156	0.016	0.01756	170

Table 3

Aggregate Risk from Chronic Dietary + Short-Term Postapplication Exposure to Turf

Subpopulation	Chronic Dietary Exposure (mg/kg/day)	Residential Turf Exposure (mg/kg/day)	Total Exposure (mg/kg/day)	MOE
U.S. Population	0.001413	1.03	1.031413	2.9
Nursing Infants	**N/A**	**N/A**	**N/A**	**N/A**
Non-Nursing Infants (<1 year old)	**0.00179**	**>4.1**	**>4.10179**	**<1.2**
Children (1-6 years old)	**0.00156**	**4.1**	**4.10156**	**1.2**
Children (7-12 years old)	**0.00118**	**<4.1**	**<4.10118**	**>1.2**
U.S. Population (Spring Season)	0.00165	1.03	1.03165	2.9
Northeast Region	0.00173	1.03	1.03173	2.9
Western Region	0.00185	1.03	1.03185	2.9
Females 13+ Years, Nursing	0.00168	1.03	1.03168	2.9
Females (20 Years and Older, Not Pregnant or Nursing)	0.00156	1.03	1.03156	2.9

Table 4

Aggregate Risk from Chronic Dietary + Dermal Short-Term Postapplication Exposure from Home Gardens and Home Orchards Treated with Vinclozolin

Subpopulation	Chronic Dietary Exposure (mg/kg/day)	Home Garden Exposure (mg/kg/day)	Total Exposure (mg/kg/day)	MOE
U.S. Population	0.001413	0.023	0.24413	120
Nursing Infants	**N/A**	**N/A**	**N/A**	**N/A**
Non-Nursing Infants (<1 year old)	**N/A**	**N/A**	**N/A**	**N/A**
Children (1-6 years old)	**0.00156**	**>0.039**	**>0.04056**	**<120**
Children (7-12 years old)	**0.00118**	**0.039**	**0.04018**	**120**
U.S. Population (Spring Season)	0.00165	0.023	0.02465	120
Northeast Region	0.00173	0.023	0.02473	120
Western Region	0.00185	0.023	0.02485	120
Females 13+ Years, Nursing	0.00168	0.023	0.02468	120
Females (20 Years and Older, Not Pregnant or Nursing)	0.00156	0.023	0.02456	120

Table 5

Aggregate Risk from Chronic Dietary + Dermal Short-Term Postapplication Exposure from U-Pick Peach and Strawberry Farms Treated with Vinclozolin

Subpopulation	Chronic Dietary Exposure (mg/kg/day)	U-Pick $\text{Exposure}_{\text{strawberries}}$ (mg/kg/day)	Total Exposure (mg/kg/day)	MOE
U.S. Population	0.001413	0.019	0.020413	150
Nursing Infants	**N/A**	**N/A**	**N/A**	**N/A**
Non-Nursing Infants (<1 year old)	**N/A**	**N/A**	**N/A**	**N/A**
Children (1-6 years old)	**0.00156**	**>0.033**	**>0.03456**	**<140**
Children (7-12 years old)	**0.00118**	**0.033**	**0.03418**	**150**
U.S. Population (Spring Season)	0.00165	0.019	0.02065	140
Northeast Region	0.00173	0.019	0.02073	140
Western Region	0.00185	0.019	0.02085	140
Females 13+ Years, Nursing	0.00168	0.019	0.02068	140
Females (20 Years and Older, Not Pregnant or Nursing)	0.00156	0.019	0.02056	150

Table 6

Aggregate Risk from Chronic Dietary + Short-Term Homeowner Handler + Dermal Short-Term Postapplication Exposure from Home Gardens and Home Orchards Treated with Vinclozolin

Subpopulation	Chronic Dietary Exposure (mg/kg/day)	Homeowner Handler Exposure (mg/kg/day)	Home Garden Exposure (mg/kg/day)	Total Exposure (mg/kg/day	MOE
U.S. Population	0.001413	0.016	0.023	0.040413	74
Nursing Infants	**N/A**	**N/A**	**N/A**	**N/A**	**N/A**
Non-Nursing Infants (<1 year old)	**N/A**	**N/A**	**N/A**	**N/A**	**N/A**
Children (1-6 years old)	**0.00156**	**N/A**	**>0.039**	**>0.04056**	**<120**
Children (7-12 years old)	**0.00118**	**N/A**	**0.039**	**0.04018**	**120**
U.S. Population (Spring Season)	0.00165	0.016	0.023	0.04065	74
Northeast Region	0.00173	0.016	0.023	0.04073	74
Western Region	0.00185	0.016	0.023	0.04085	73
Females 13+ Years, Nursing	0.00168	0.016	0.023	0.04068	74
Females (20 Years and Older, Not Pregnant or Nursing)	0.00156	0.016	0.023	0.04056	74

Chronic Aggregate Risk

The aggregate chronic risk is equal to the sum of the chronic risk from food + water + residential uses. According to a search of the Reference File Systems (REFS) on 04/29/97, vinclozolin is not currently registered for any indoor residential uses. The outdoor non-food residential uses include ornamental flowering plants and ornamental turf. These outdoor uses would not fall under a chronic scenario. Therefore, the aggregate chronic risk for vinclozolin is equal to the sum of the chronic risk from food + water, and is equivalent to the following percentages of the RfD:

Subpopulation	food	water	TOTAL
U.S. Population	12%	< 1%	< 13%
Nursing Infants	**7%**	**< 1%**	**< 8%**
Non-Nursing Infants (<1 year old)	**14%**	**< 1%**	**< 15%**
Children (1-6 years old)	**12%**	**< 1%**	**< 13%**
Children (7-12 years old)	**9%**	**< 1%**	**< 10%**
U.S. Population (Spring Season)	14%	< 1%	< 15%
Northeast Region	14%	< 1%	< 15%
Western Region	15%	< 1%	< 16%
Females 13+ Years, Nursing	14%	< 1%	< 15%
Females (20 Years and Older, Not Pregnant or Nursing)	13%	< 1%	< 14%

Cancer Aggregate Risk

The Cancer Peer Review Committee (CPRC) met on 1/15/97 (3rd Meeting, memo dated 4/3/97) to re-evaluate the carcinogenic potential of vinclozolin, based on revised pathology results. The

majority of the CPRC agreed that vinclozolin should be classified as Group C - possible human carcinogen, with a non-linear approach (MOE) based on a NOEL of 4.9 mg/kg/day for hormone-related effects (decreased epididymal weight at 30 mg/kg/day) in the 2-generation oral rat reproduction study to quantify human risk. The MOE approach was chosen because the remaining tumors (Leydig cell) were benign at dose levels which were not considered to be excessive, and there was little concern for mutagenicity of vinclozolin.

According to a search of the Reference File Systems (REFS) on 04/29/97, vinclozolin is not currently registered for any indoor residential uses. The outdoor non-food residential uses include ornamental flowering plants and ornamental turf. These outdoor uses would not fall under a chronic cancer scenario. Therefore, the aggregate cancer risk for vinclozolin is equal to the sum of the chronic risk from food + water. The Anticipated Residue Contribution (ARC) from the chronic DRES analysis for the U.S. Population was calculated to be 0.001383 mg/kg/day from food and 0.0000303 from dietary water, for a total dietary exposure (food + water) of 0.001413. Using the formula where the Margin of Exposure (MOE) = NOEL (mg/kg/day) ÷ Exposure (mg/kg/day), or 4.9 mg/kg/day ÷ 0.001413 mg/kg/day, the calculated **MOE (food + water) is 3,500.**

Cumulative Effects

Vinclozolin is a member of the imides class of fungicides/bactericides. Other members of the imides include iprodione and procymidone.

However, the Agency has not made a determination whether vinclozolin and any other pesticide have a common mode of toxicity and require cumulative risk assessment. For the purposes of this Section 3 registration, the Agency has considered only risks from vinclozolin. If required, cumulative risks will be assessed as part of Reregistration and tolerance reassessment, and when methodologies for determining common mode of toxicity and for performing cumulative risk assessment are finalized.

Determination of Safety for Infants and Children

The pre- and post-natal toxicology data base for vinclozolin is complete with respect to current toxicological data requirements. In a meeting held on 1/23/97 (memo of W. Burnam dated 2/21/97 - see Attachment IV), members of HED decided that extra (greater than 100) uncertainty factors were <u>not</u> appropriate when used with the developmental toxicity endpoint of 3 mg/kg/day.

SUPPLEMENTAL INFORMATION

DETAILED CONSIDERATIONS

OCCUPATIONAL EXPOSURE

Table 7. Intermediate-term REI calculations for snap beans[a].

DAT	FDR ($\mu g/cm^2$)[b]	Exposure (mg/day)[c]	Dose (mg/kg/day)[d]	MOE[e]
0	1.2327	9.8616	0.04109	73
1	1.0622	8.4976	0.03541	85
2	0.9194	7.3552	0.03065	98
3	0.7994	6.3952	0.02665	110

[a] Best Fit FDR ($\mu g/cm^2$) = foliar dislodgeable residue; double sided leaves. The Transfer Coefficient (TC) in the original study was 749 cm^2/hr, for this evaluation, a TC of 1000 cm^2/hr was used. See attached OREB review, Table 10 (01/30/96, J. Leahy/OREB to D. Edwards/RCAB).

[b] Exposure (mg/day) = [(Best Fit FDR x Transfer Coefficient (1000 cm^2/hr)) ÷ 1000] x 8 hrs.

[c] Dose (mg/kg/day) = Exposure/60 kg x Dermal Absorption Rate (25%)

[d] MOE = NOEL (3.0 for short & intermediate-term exposure) ÷ Dose

[e] MOE, expressed to two significant figures, is based on the average of FDR data on DAT 0, 1, 2, and 3.

Table 8. Occupational Exposure Assumptions	
PARAMETER	**ASSUMPTION**
Pesticide Handlers Exposure Database (PHED), Version 1.1.; Unit of exposure values for mixer/loaders from DF.OPN.MLOD (7/96); Unit of exposure values for groundboom applicators from GBM.OPN.APPL (7/96); Unit of exposure values for aerial applicators from Best Available Surrogate Exposure Table (BASET, 7/25/96)	Mixer/Loader: Dermal exposure [dry flowable, open pour, two layers clothing (arithmetically corrected-50%) plus gloves] = 44.2969 μg ai/lb handled; Inhalation exposure (arithmetically corrected for dust/mist respirator-80%) = 0.1537 μg ai/lb handled.
	Applicator: Dermal exposure [groundboom, open cab, two layers clothing (arithmetically corrected-50%) plus gloves] = 11.2678 μg ai/lb applied; Inhalation exposure (arithmetically corrected for dust/mist respirator-80%) = 0.1479 μg ai/lb handled.
	Applicator: Dermal exposure (aerial, liquid formulations, enclosed cockpit, single layer clothing, no gloves) = 5.0 μg ai/lb applied; Inhalation exposure = 0.068 μg ai/lb handled.
Dermal absorption	Dermal = 25% (Tox value); Inhalation = 100% (default).
Application type	Groundboom and air
Minimum Finish Spray	Ground: 40 gal/A; Air: 5 gal/A
Maximum Application rate	0.5 lbs ai/A
Duration of Occupational Exposure	Intermediate (one week to several months)
Maximum Applications per year	2
Acres treated/day (Y. NG, BEAD)	Ground: 64 acres; Air: 351
Worker Weight	60 kg (based on Tox endpoint)
Number of Farms Treated	Ground: 2; Air: 10 (OREB default values for PCOs)

Table 9. Occupational Exposure and Risk Assessment[a]		
Worker	**Short & Intermediate-Term Dermal + Inhalation[b] (ug/kg/day)**	**Short & Intermediate-Term MOE[c]**
Ground Mixer/Loader	5.99	500
Air Mixer/Loader	32.84	91
Ground Applicator	1.58	1,900
Air Applicator	3.86	780

a MOEs are expressed to two significant figures.

b Average Daily Dose (ADD) Short & Intermediate-Term = PHED unit exposure (dermal x % absorption + inhalation x % absorption) x application rate x acres treated/day ÷ kg body weight.

c Short & Intermediate-term occupational exposure MOE = NOEL/ADD (where NOEL = 3 mg/kg/day).

Dietary Exposure

Table 10. Residue Consideration Summary Table		
PARAMETER	**PROPOSED USE**	**RESIDUE DATA**
CHEMICAL	vinclozolin	vinclozolin
FORMULATION	RONILAN DF	RONILIN WP
CROP	snap beans	snap beans and lima beans
TYPE APPLICATION	ground or air	ground, air, and chemigation
# APPLICATIONS	up to 2	2
TIMING	postemergence (1st application at early bloom stage; 2nd application at full bloom (7 to 21 days after 1st application)	2 treatments made 7 days apart, 14-day PHI for the last treatment
RATE/APPLICATION	0.5 lbs ai/A (1 lb formulation)	1.0 lbs ai/A
RATE/YEAR or SEASON	1.0 lbs ai/A/season	2.0 lbs ai/A/crop
RESIDUE DATA	N/A	See Tables 11 and 12
RESTRICTIONS	Do not apply within 9 days of harvest. Do not make more than 2 applications per season Do not apply more than 2 lbs of RONILAN DF per acre per season When applying RONILAN DF by ground equipment, apply in a minimum of 40 gallons of water per acre When applying RONILAN DF by air, use less than 20 gallons of spray solution per acre Do not feed dry forage (bean hay from treated fields) to livestock or permit livestock to graze in treated fields. Do not feed succulent green bean seed from treated fields to poultry or livestock.	
RESIDUE DATA SOURCE	N/A	PP#9F3762 (memo of R.W. Cook dated 8/18/92 - MRID#410806-01)
PERFORMING LAB	N/A	Hazleton Laboratories, Madison WI

Additional Information

The following data were reviewed in conjunction with PP#9F3762 (memo of R.W. Cook dated 8/18/92 - MRID#410806-01):

Sixteen (16) residue trials were conducted in a total of 7

states. Each trial consisted of a single residue sample. The residue trials were conducted using the RONILIN WP formulation. Eight of the trials involved application to lima beans and eight to snap beans. Ground applications were made in approximately 50 gallons of finish spray per acre; air applications in 5 to 15 gallons per acre. Samples of beans, cannery waste, green forage, and dry forage were analyzed, but only the results from the snap bean beans are presented due to changes in Table 1 of OPPTS 860.1000. The results are shown in Table 11.

Table 11

field trial location	application type	bean type	residue found (ppm)
NC	ground	snap	0.62
NY			0.38
FL			0.53
MI			0.73
CA			2.40
MI	aerial	snap	0.64
NY			0.76
OR	chemigation	snap	0.95

The following data were previously submitted to the Agency but had not been reviewed until this time.

"Magnitude of Vinclozolin Residue for Snap Beans: WP vs. DF Formulation - Ground Application", G.S. Sotack and S.H. Jackson, 8/17/94, BASF Corp., Study# 92028 (MRID# 435059-03)

Crop field trials were conducted at four sites in three states in order to bridge the DF formulation to the WP formulation by comparing residues of samples from trials that included plots treated with each formulation. Each plot received two applications of the test substance; one application at the "beginning bloom" stage and one application 14 days before harvest. The target rate for each application was 1.0 lb.ai./A., which is 2X the proposed rate. Preharvest intervals were 14 days for all samples (vs. 9 days on the proposed label). Average recovery for all analyses was 97±10% (n = 14). The results of the analyses are shown in Table X.

Table 12

Residues of Vinclozolin in/on Snap Beans

site	formulation	rate	PHI	residue (ppm)
California (1)	DF	2 applications at 1.0 lbs.ai./A./application	14 days	0.96 0.95 1.03 0.91 0.94 1.09 0.83 0.73 1.06
	WP			1.25 1.84 1.03 1.39 1.04 0.88 0.94 1.31 1.80 1.99 1.08 1.60
California (2)	DF			1.25 1.22 1.17
	WP			0.96 1.15 1.18
New York	DF			0.29 0.35 0.29 0.42
	WP			0.28 0.30 0.41 0.46
North Carolina	DF			0.66 0.63 0.67 0.61
	WP			0.65 0.62 0.57

Field trial residue studies conducted in California exhibit higher residues (up to 2.4 ppm) than those from other states (NY - up to 0.76 ppm; NC - up to 0.67 ppm; FL - up to 0.53 ppm; MI - up to 0.73 ppm; and OR - up to 0.95 ppm). None of the field trial residue data mimic that of the proposed use - the field trial rates were all double the proposed use (1.0 lb.ai./A./application vs. 0.5) and the PHIs were longer (typically 14 days in the field trials and a proposed PHI of 9 days). This may be due to the decreased rainfall in CA, coupled with the extensive use of ground irrigation (rather than overhead irrigation). California has never requested or been granted a Section 18 for use of vinclozolin on snap beans. Requests have been received from the following states:

MI, MN, NY, OR, PA, WA, and WI (personal conversation with Libby Pemberton, ERMUS/RD/OPP).

A CODEX MRL for residues of vinclozolin and its metabolites containing the 3,5-dichloroaniline moiety has been established for common beans at 2.0 ppm. Residue data were examined at the Joint meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues, Rome, 9/29-10/8/86. The field trials were conducted in Germany, the Netherlands, Japan, United Kingdom, and France. At the meeting, it was decided that a 2.0 ppm MRL should be established based on rates of 0.19 (3 applications) to 1.0 kg.ai./ha. (3 applications) and a PHI of 7 days. These rates are equivalent to 0.17 to 0.89 lbs.ai./A.

In light of harmonizing with CODEX, examining the CODEX field trial data (including application rates and PHIs), and examining the U.S. data where vinclozolin will be used (including application rates and PHIs), PIRAT believes that a 2.0 ppm tolerance is appropriate for domestic snap beans.

Attachment I: memo of D.G. Anderson dated 4/30/97
Attachment II: Chronic DRES Analyses (4/27/97)
Attachment III: memo of R.D. Jones dated 2/27/97
Attachment IV: memo of W. Burnam dated 2/21/97

cc (with Attachments): Herndon, PIRAT, J. Leahy (OREB), Chemistry PP#9F3763, DRES (B. Steinwand), K. Boyle (RCAB), Robert Perlis, OGC (2333).

cc (without Attachments): Dykstra, Lewis, Caswell File (#323C), D. Anderson (TOX).

RDI:PIRAT: 5/8/97

Attachment I Jeff H

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

OFFICE OF PREVENTION, PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM:

Subject: Dietary and residential exposure endpoints for acute, short term, and intermediate exposure from vinclozolin.

From: David G Anderson David G Anderson 4/30/97
Toxicology Branch-1
HED (7509C)

To: Kathryn Boyle
Chemical Coordination Branch
HED (7509C)

Karl Baetcke, William Burnam, Kathryn Boyle and David Anderson met at 3:00 PM on 4/17/97 to determine appropriate endpoints for acute dietary and acute and intermediate residential exposure to vinclozolin. This action affects only residential exposures for infants and children 1-12 years of age. This *ad hoc* meeting was designed principally to address potential problems in assessing hazards associated with treatment of recreational areas, lawns and other home uses of vinclozolin. For FQPA purposes, Acute Dietary exposure endpoints and Short Term and Intermediate Term residential exposure endpoints for infants and children less than 12 years of age are required.

(1) Acute Dietary Endpoint (infants and children 1-12 years of age): None.

[Note: The current Acute Dietary endpoint of 3 mg/kg/day NOEL (endpoint should be adjusted to 5.5 mg/kg for the pharmacokinetics of vinclozolin) for developmental effects (AGD) still holds for reproductive age females 13 and over, the only appropriate subpopulation.]

No toxicity was observed in any study that was appropriate for an Acute Dietary endpoint for infants and children 1-12 years old including acute LD50 studies.

(2) Short Term (1-7 days) and Intermediate Term (one week to several months) Residential exposure for infants and children 1-12 only): The LOEL is 15 mg/kg/day (oral) based on delayed puberty in rats with the NOEL of 5 mg/kg/day (oral). These values should be corrected for dermal penetration of about 25%. Since the effect is delayed puberty, the only appropriate subpopulation to which this endpoint should be applied is infants and children 1-12

years old. (Data from Earl Gray's presentation to the '96 SAP for vinclozolin.)

[Note: The TES document selected a NOEL of 3 mg/kg/day from a developmental study (AGD) (corrected for dermal penetration) as an endpoint for Short Term and Intermediate Term Occupational and Residential exposure. It was considered protective of females 13 years old and older that may be part of the work force and it would also be protective in the case of residential dermal exposure after adjustment for dermal penetration.]

Attendees:

1. Karl Baetcke: _____, Date 5/5/97

2. William Burnam: _____, Date 5/6/97

3. Kathryn Boyle: _____, Date 5/6/97

4. David G Anderson: _____, Date 4/30/97

Signature indicates agreement with endpoints selected above.

Notes on the Data Used:

The data on delayed puberty was conducted at RTP by Gray et al. and presented to the SAP 10/30/96. It may be published by now. Delayed puberty occurred in the animals dosed for about 20 days at 15 mg/kg/day with a NOEL of 5 mg/kg/day.

Long Evans Hooded rats were exposed to vinclozolin by gavage from weaning to 15 weeks of age at dose levels of 0, 5, 15, 25 or 100 mg/kg/day. (numbers of animals used were unspecified, but were probably in the range of 5 to 15 males and females per group). A measure of puberty (age at preputial separation) was delayed (≈ 1 day) (control 40.7 days and 41.8 days at 15 mg/kg/day, $p \leq 0.05$) in treated males at 15 mg/kg/day. This is supported by reduced epididymal weight in males at 15 mg/kg/day at termination (the NOEL is 5 mg/kg/day) and a reduced epididymal weight in P0 males from a two-generation reproduction study with a NOEL of 4.9 mg/kg/day. Although, the slightly delayed puberty is of unknown consequence, it probably resulted from androgen deprivation from weaning to about day 40, during growth and development.

Memo short and intermediate term residential exposure/A:\ACUINTE2.EPT/DANDERSON/4/30/97.*

CHEMICAL INFORMATION	STUDY TYPE	EFFECTS	REFERENCE DOSES	DATA GAPS/COMMENTS	STATUS
Vinclozolin (Ronilan) Caswell #323C CAS No. 50471-44-8 A.I. CODE: 113201 CFR No. 180.380 185.1850	2yr feeding- rat NOEL= 1.2000 mg/kg 25.00 ppm LEL= 2.3000 mg/kg 50.00 ppm ONCO: E (HED)	Eosinophilic foci in the liver & foam cell aggregates in lungs (M); lenticular degeneration & interstitial cell lipidosis in ovaries (F).	ADI UF -->100 OPP RfD= 0.012000 EPA RfD= 0.025000	No data gaps.	HED reviewed 05/19/86 EPA verified 07/08/86 WHO reviewed 1988 RfD/PR reviewed 08/03/95 On IRIS.

POPULATION SUBGROUP	TOTAL TMRC (MG/KG BODY WEIGHT/DAY) CURRENT TMRC*	NEW TMRC**	NEW TMRC AS PERCENT OF RFD	DIFFERENCE AS PERCENT OF RFD	EFFECT OF ANTICIPATED RESIDUES ARC	%RFD
U.S. POPULATION - 48 STATES	0.018806	0.019703	164.191442	7.471117	0.001383	11.52681
U.S. POPULATION - SPRING SEASON	0.018763	0.019620	163.497475	7.140800	0.001622	13.51815
U.S. POPULATION - SUMMER SEASON	0.024215	0.025186	209.883542	8.090075	0.001326	11.05372
U.S. POPULATION - FALL SEASON	0.016261	0.017110	142.585983	7.079450	0.001141	9.50928
U.S. POPULATION - WINTER SEASON	0.016002	0.016810	140.080625	6.727783	0.001259	10.49442
NORTHEAST REGION	0.020460	0.021177	176.476425	5.979000	0.001695	14.12174
NORTH CENTRAL REGION	0.019098	0.019884	165.696783	6.543600	0.001199	9.99541
SOUTHERN REGION	0.014526	0.015671	130.590850	9.539233	0.000898	7.48175
WESTERN REGION	0.023580	0.024309	202.572800	6.075392	0.001822	15.18068
HISPANICS	0.021377	0.021897	182.470892	4.326408	0.000950	7.91524
NON-HISPANIC WHITES	0.019661	0.020526	171.045867	7.205717	0.001475	12.28887
NON-HISPANIC BLACKS	0.012334	0.013408	111.733217	8.948525	0.000640	5.33216
NON-HISPANIC OTHERS	0.016506	0.017418	145.148208	7.595792	0.001299	10.82408
NURSING INFANTS (< 1 YEAR OLD)	0.044185	0.045220	376.836375	8.624117	0.000867	7.22767
NON-NURSING INFANTS (< 1 YEAR OLD)	0.089879	0.092783	773.195183	24.201508	0.001679	13.99278
FEMALES (13+ YEARS, PREGNANT)	0.016335	0.016772	139.767475	3.641042	0.001068	8.89984
FEMALES 13+ YEARS, NURSING	0.018154	0.018796	156.633617	5.348667	0.001645	13.71229
CHILDREN (1-6 YEARS OLD)	0.037154	0.038752	322.937000	13.322208	0.001455	12.12357
CHILDREN (7-12 YEARS OLD)	0.024579	0.025751	214.588808	9.765258	0.001075	8.95831
MALES (13-19 YEARS OLD)	0.013610	0.014391	119.923183	6.510150	0.000752	6.27044
FEMALES (13-19 YEARS OLD, NOT PREG. OR NURSING)	0.013373	0.014052	117.102942	5.662592	0.000757	6.30940
MALES (20 YEARS AND OLDER)	0.013791	0.014496	120.798450	5.870317	0.001439	11.98774
FEMALES (20 YEARS AND OLDER, NOT PREG. OR NURS)	0.015745	0.016465	137.207600	5.995517	0.001526	12.71677

*Current TMRC does not include new or pending tolerances.
**New TMRC includes new, pending, and published tolerances.

Attachment II

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TOLERANCE ASSESSMENT SUMMARY FOR Vinclozolin (Ronilan) DATE: 04/25/97
USING ANTICIPATED RESIDUES
CASWELL #323C

ANALYSIS FOR POPULATION SUB-GROUP: U.S. POPULATION - 48 STATES

EXISTING ANTICIPATED RESIDUES (PUBLISHED ONLY)		
RESULT IN AN ARC OF:	0.001154	MG/KG/DAY
THE EXISTING ARC IS EQUIVALENT TO:	9.615	% OF THE ADI.
PROPOSED NEW ANTICIPATED RESIDUES (CURRENT PETITION ONLY)		
RESULT IN AN ARC OF:	0.000046	MG/KG/DAY
THESE NEW ANTICIPATED RESIDUES WILL OCCUPY:	0.387	% OF THE ADI.
IF THE NEW ANTICIPATED RESIDUES (CURRENT PETITION ONLY)		
ARE APPROVED THE RESULTANT ARC WILL BE:	0.001200	MG/KG/DAY
THE NEW ARC WILL OCCUPY	10.002	% OF THE ADI.
OTHER PENDING ANTICIPATED RESIDUES EXCLUDING THE		
CURRENT NEW PETITION HAVE AN ARC OF:	0.000183	MG/KG/DAY
THIS ARC WILL OCCUPY	1.525	% OF THE ADI.
IF ALL PENDING ANTICIPATED RESIDUES (INCLUDING THE		
CURRENT NEW PETITION) ARE GRANTED		
THE RESULTANT ARC WILL BE:	0.001383	MG/KG/DAY
THE TOTAL ARC WILL OCCUPY	11.527	% OF THE ADI.

ANALYSIS FOR POPULATION SUB-GROUP: NON-NURSING INFANTS (< 1 YEAR OLD)

EXISTING ANTICIPATED RESIDUES (PUBLISHED ONLY)		
RESULT IN AN ARC OF:	0.001471	MG/KG/DAY
THE EXISTING ARC IS EQUIVALENT TO:	12.259	% OF THE ADI.
PROPOSED NEW ANTICIPATED RESIDUES (CURRENT PETITION ONLY)		
RESULT IN AN ARC OF:	0.000170	MG/KG/DAY
THESE NEW ANTICIPATED RESIDUES WILL OCCUPY:	1.413	% OF THE ADI.
IF THE NEW ANTICIPATED RESIDUES (CURRENT PETITION ONLY)		
ARE APPROVED THE RESULTANT ARC WILL BE:	0.001641	MG/KG/DAY
THE NEW ARC WILL OCCUPY	13.672	% OF THE ADI.
OTHER PENDING ANTICIPATED RESIDUES EXCLUDING THE		
CURRENT NEW PETITION HAVE AN ARC OF:	0.000039	MG/KG/DAY
THIS ARC WILL OCCUPY	0.321	% OF THE ADI.
IF ALL PENDING ANTICIPATED RESIDUES (INCLUDING THE		
CURRENT NEW PETITION) ARE GRANTED		
THE RESULTANT ARC WILL BE:	0.001679	MG/KG/DAY
THE TOTAL ARC WILL OCCUPY	13.993	% OF THE ADI.

ANTICIPATED RESIDUE INFORMATION FOR CASWELL NUMBER 323C DATE: 04/25/97 PAGE: 1

CHEMICAL	STUDY TYPE	EFFECTS	REFERENCE DOSES	DATA GAPS/COMMENTS	STATUS
Vinclozolin (Ronilan) Caswell #323C CAS No. 50471-44-8 A.I. CODE: 113201 CFR No. 180.380 185.1850	2yr feeding- rat NOEL= 1.2000 mg/kg 25.00 ppm LEL= 2.3000 mg/kg 50.00 ppm ONCO: E (HED)	Eosinophilic foci in the liver & foam cell aggregates in lungs (M); lenticular degeneration & interstitial cell lipidosis in ovaries (F).	ADI UF -->100 OPP RfD= 0.012000 EPA RfD= 0.025000	No data gaps.	HED reviewed 05/19/86 EPA verified 07/08/86 WHO reviewed 1988 RfD/PR reviewed 08/03/95 On IRIS.

FOOD CODE	FOOD	FOOD FORM	PET.#	TOLERANCE (ppm)	ANTICIPATED RESIDUE (ppm)	AR STATISTIC TYPE	% CROP TREATED	RES. VALUE USED IN TAS RUN (ppm)
01002AA	BLACKBERRIES	10 RAW-FRESH OR NFS	0E3903	A 10.00000	10.000000		100.00	10.000000
01002AA	BLACKBERRIES	21 COOKED-NFS	0E3903	A 10.00000	10.000000		100.00	10.000000
01002AA	BLACKBERRIES	62 COOKED-FRESH OR FROZEN-BAKED	0E3903	A 10.00000	10.000000		100.00	10.000000
01003AA	BOYSENBERRIES	10 RAW-FRESH OR NFS	0E3903	A 10.00000	10.000000		100.00	10.000000
01004AA	DEWBERRIES	00 NOT SPECIFIED (NO CONSUMPTION)	0E3903	A 10.00000	10.000000		100.00	10.000000
01005AA	LOGANBERRIES	00 NOT SPECIFIED (NO CONSUMPTION)	0E3903	A 10.00000	10.000000		100.00	10.000000
01006AA	RASPBERRIES	10 RAW-FRESH OR NFS	3F2934	P 5.000000	5.000000		45.00	2.250000
01006AA	RASPBERRIES	15 RAW-FRESH OR CANNED	3F2934	P 5.000000	5.000000		45.00	2.250000
01006AA	RASPBERRIES	31 COOKED-FRESH OR CANNED	3F2934	P 5.000000	5.000000		45.00	2.250000
01006AA	RASPBERRIES	62 COOKED-FRESH OR FROZEN-BAKED	3F2934	P 5.000000	5.000000		45.00	2.250000
01006AA	RASPBERRIES	70 RAW-FROZEN	3F2934	P 5.000000	5.000000		45.00	2.250000
01010AA	CRANBERRIES	10 RAW-FRESH OR NFS	4F3237	A 2.000000	2.000000		100.00	2.000000
01010AA	CRANBERRIES	21 COOKED-NFS	4F3237	A 2.000000	2.000000		100.00	2.000000
01010AA	CRANBERRIES	31 COOKED-FRESH OR CANNED	4F3237	A 2.000000	2.000000		100.00	2.000000
01010JA	CRANBERRY-JUICE	15 RAW-FRESH OR CANNED	4F3237	A 2.000000	2.000000		100.00	2.000000
01010JA	CRANBERRY-JUICE	31 COOKED-FRESH OR CANNED	4F3237	A 2.000000	2.000000		100.00	2.000000
01016AA	STRAWBERRIES	10 RAW-FRESH OR NFS	9F2205	P 10.00000	10.000000		63.00	6.300000
01016AA	STRAWBERRIES	21 COOKED-NFS	9F2205	P 10.00000	10.000000		63.00	6.300000
01016AA	STRAWBERRIES	70 RAW-FROZEN	9F2205	P 10.00000	10.000000		63.00	6.300000
05001AA	APRICOTS-FRESH	10 RAW-FRESH OR NFS	2F2650	P 5.000000	5.000000		5.00	0.250000
05001AA	APRICOTS-FRESH	21 COOKED-NFS	2F2650	P 5.000000	5.000000		5.00	0.250000
05001AA	APRICOTS-FRESH	31 COOKED-FRESH OR CANNED	2F2650	P 5.000000	5.000000		5.00	0.250000
05001DA	APRICOTS-DRIED	10 RAW-FRESH OR NFS	2F2650	P 5.000000	5.000000		5.00	0.250000
05001DA	APRICOTS-DRIED	22 COOKED-FRESH-BAKED	2F2650	P 5.000000	5.000000		5.00	0.250000
05002AA	CHERRIES-FRESH	10 RAW-FRESH OR NFS	2F2650	P 5.000000	5.000000		5.00	0.250000
05002AA	CHERRIES-FRESH	21 COOKED-NFS	2F2650	P 5.000000	5.000000		5.00	0.250000
05002AA	CHERRIES-FRESH	31 COOKED-FRESH OR CANNED	2F2650	P 5.000000	5.000000		5.00	0.250000
05002AA	CHERRIES-FRESH	62 COOKED-FRESH OR FROZEN-BAKED	2F2650	P 5.000000	5.000000		5.00	0.250000
05002DA	CHERRIES-DRIED	00 NOT SPECIFIED	2F2650	P 5.000000	5.000000		5.00	0.250000
05002JA	CHERRIES-JUICE	15 RAW-FRESH OR CANNED	2F2650	P 5.000000	5.000000		5.00	0.250000
05002JA	CHERRIES-JUICE	21 COOKED-NFS	2F2650	P 5.000000	5.000000		4.00	0.200000
05003AA	NECTARINES	10 RAW-FRESH OR NFS	2F2650	P 5.000000	5.000000		11.00	0.550000
05004AA	PEACHES-FRESH	10 RAW-FRESH OR NFS	2F2650	P 5.000000	5.000000		11.00	0.550000
05004AA	PEACHES-FRESH	21 COOKED-NFS	2F2650	P 5.000000	5.000000		11.00	0.550000
05004AA	PEACHES-FRESH	31 COOKED-FRESH OR CANNED	2F2650	P 5.000000	5.000000		11.00	0.550000
05004AA	PEACHES-FRESH	51 COOKED-CANNED	2F2650	P 5.000000	5.000000		11.00	0.550000
05004DA	PEACHES-DRIED	10 RAW-FRESH OR NFS	2F2650	P 5.000000	5.000000		11.00	0.550000
05004DA	PEACHES-DRIED	21 COOKED-NFS	2F2650	P 5.000000	5.000000		11.00	0.550000
06018AA	KIWI	10 RAW-FRESH OR NFS	0E2380	P 10.00000	10.000000		100.00	10.000000
10010AA	CUCUMBERS	10 RAW-FRESH OR NFS	8E3688	P 1.000000	1.000000		35.00	0.350000

ANTICIPATED RESIDUE INFORMATION FOR CASWELL NUMBER 323C DATE: 04/25/97 PAGE: 2

CHEMICAL	STUDY TYPE	EFFECTS	REFERENCE DOSES	DATA GAPS/COMMENTS	STATUS
Vinclozolin (Ronilan) Caswell #323C CAS No. 50471-44-8 A.I. CODE: 113201 CFR No. 180.380 185.1850	2yr feeding- rat NOEL= 1.2000 mg/kg 25.00 ppm LEL= 2.3000 mg/kg 50.00 ppm ONCO: E (HED)	Eosinophilic foci in the liver & foam cell aggregates in lungs (M); lenticular degeneration & interstitial cell lipidosis in ovaries (F).	ADI UF -->100 OPP RfD= 0.012000 EPA RfD= 0.025000	No data gaps.	HED reviewed 05/19/86 EPA verified 07/08/86 WHO reviewed 1988 RfD/PR reviewed 08/03/95 On IRIS.

FOOD CODE	FOOD	FOOD FORM	PET.#	TOLERANCE (ppm)	ANTICIPATED RESIDUE (ppm)	AR STATISTIC TYPE	% CROP TREATED	RES. VALUE USED IN TAS RUN (ppm)
10010AA	CUCUMBERS	11 RAW-FRESH-PICKLED,CORNED OR CURED	8E3688	P 1.000000	1.000000		35.00	0.350000
10010AA	CUCUMBERS	21 COOKED-NFS	8E3688	P 1.000000	1.000000		35.00	0.350000
11003AA	PEPPERS,SWEET	10 RAW-FRESH OR NFS	4E2998	P 3.000000	3.000000		20.00	0.600000
11003AA	PEPPERS,SWEET	21 COOKED-NFS	4E2998	P 3.000000	3.000000		20.00	0.600000
13003AA	CHICORY	10 RAW-FRESH OR NFS	8E3620	P 2.000000	2.000000		100.00	2.000000
13013AA	LETTUCE-LEAFY	10 RAW-FRESH OR NFS	3F2934	P 10.00000	10.000000		9.00	0.900000
13015AA	ENDIVE	10 RAW-FRESH OR NFS	8E3688	P 2.000000	2.000000		100.00	2.000000
13015AA	ENDIVE	21 COOKED-NFS	8E3688	P 2.000000	2.000000		100.00	2.000000
13020AA	LETTUCE-UNSPEC	10 RAW-FRESH OR NFS	2F2595	P 10.00000	10.000000		9.00	0.900000
13045AA	LETTUCE-HEAD	10 RAW-FRESH OR NFS	2F2595	P 10.00000	10.000000		9.00	0.900000
13045AA	LETTUCE-HEAD	21 COOKED-NFS	2F2595	P 10.00000	10.000000		9.00	0.900000
14007AA	GARLIC	10 RAW-FRESH OR NFS	3F2934	P 6.000000	6.000000		100.00	6.000000
14007AA	GARLIC	21 COOKED-NFS	3F2934	P 6.000000	6.000000		100.00	6.000000
14007AA	GARLIC	32 COOKED-FRESH OR CANNED-BAKED	3F2934	P 6.000000	6.000000		100.00	6.000000
14011AA	ONIONS-DRY-BULB	10 RAW-FRESH OR NFS	3F2934	P 6.000000	6.000000		5.00	0.300000
14011AA	ONIONS-DRY-BULB	21 COOKED-NFS	3F2934	P 6.000000	6.000000		5.00	0.300000
14011AA	ONIONS-DRY-BULB	22 COOKED-FRESH-BAKED	3F2934	P 6.000000	6.000000		5.00	0.300000
14011AA	ONIONS-DRY-BULB	31 COOKED-FRESH OR CANNED	3F2934	P 6.000000	6.000000		5.00	0.300000
14011DA	ONIONS-DRIED	12 RAW-FRESH-DRIED	3F2934	P 6.000000	6.000000		5.00	0.300000
14017AA	SHALLOTS	00 NOT SPECIFIED (NO CONSUMPTION)	3F2934	P 6.000000	6.000000		100.00	6.000000
15003AA	BEANS-SUCC-GREEN	21 COOKED-NFS	9F3762	N 2.000000	2.000000		10.00	0.200000
15003AB	BEANS-SUCC-OTH	10 RAW-FRESH OR NFS	9F3762	N 2.000000	2.000000		10.00	0.200000
15003AB	BEANS-SUCC-OTH	21 COOKED-NFS	9F3762	N 2.000000	2.000000		10.00	0.200000
15003AC	BEANS-SUCC-WAX	21 COOKED-NFS	9F3762	N 2.000000	2.000000		10.00	0.200000
43058AA	WINE AND SHERRY	10 RAW-FRESH OR NFS	1E2457	P 6.000000	6.000000		100.00	6.000000
43058AA	WINE AND SHERRY	21 COOKED-NFS	1E2457	P 6.000000	6.000000		100.00	6.000000

Attachment III

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

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

MEMORANDUM February 27, 1997

SUBJECT: Tier 1 Estimated Environmental Concentrations for Vinclozolin
PC Code: 113201

TO: Jeffery Herndon, Chemist
PIRAT

FROM: R. David Jones, Ph.D., Agronomist
Special Review Section

THROUGH: William Hazel, Ph.D.,
Section Head
Special Review Section

This memo describes the Tier 1 Estimated Environmental Concentrations (EEC's) calculated with GENEEC for use in human health risk assessments for vinclozolin. These values represent upper bound estimates of the concentration that might be found in surface water due to the use of vinclozolin. The acute EEC is 27.04 $\mu g\ L^{-1}$ and the chronic EEC is 1.06 $\mu g\ L^{-1}$. These values are appropriate to reflect use on snap beans.

GENEEC is a screening model designed by Ron Parker of the Surface Water Section (Parker, 1996) of Environmental Fate and Ground Water Branch of the Office of Pesticide Programs to estimate the concentrations found in water for use in ecological risk assessment. As such, it provides upper bound values on the concentrations that might be found in the ecologically sensitive environments due to the use of a pesticide. It was designed to be simple to use and to only require data which is typically available early in the pesticide registration process. GENEEC is a single event model (one runoff event), but can account for spray drift from multiple applications. GENEEC is hardwired to represent a 10 ha field immediately adjacent to a 1 ha pond, 2 m deep with no outlet. The pond receives a spray drift event from each application plus one runoff event. The runoff event moves a maximum of 10% of the applied pesticide into the pond. This amount can be reduced due to degradation on the field and the effects of binding to soil in the field. Spray drift is equal to 1%

of the applied for ground spray application.

GENEEC is not an ideal tool for use in drinking water risk assessment. Surface-water-source drinking water tends to come from bodies of water that are substantially larger than a 1 hectare pond. Furthermore, GENEEC assumes that essentially the whole basin receives an application of the chemical. In virtually all cases, basins large enough to support a drinking water facility will contain a substantial fraction of area which does not receive the chemical. Furthermore there is always at least some flow (in a river) or turn over (in a reservoir or lake) of the water so the persistence of the chemical near the drinking water facility is usually overestimated. Given all this, GENEEC does provide an upper bound on the concentration of pesticide that could be found in drinking water and therefore can be appropriately used in screening calculations. If a risk assessment performed using GENEEC output does not exceed the level of concern, then one can be reasonably confident that the actual risk will not be exceeded. However, since GENEEC can substantially overestimate true drinking water concentrations, it will be necessary to refine the GENEEC estimate if the level of concern is exceeded. There are a variety of potential methods available. When the level of concern is exceeded and the GENEEC value is a substantial part of the total exposure, please contact me and I will assist in arranging further refinement of the exposure. In this case, a Tier 2 estimate using a scenario appropriate for snap beans would likely show that the amount of vinclozolin reaching surface water is substantially less than is estimated with GENEEC.

The input values for GENEEC are listed in Table 1. The aerobic soil metabolism value was multiplied by three to account for the uncertainty due to there only being a single measurement. The hydrolysis half-life is estimated from a regression analysis using all the available hydrolysis data rather than on the measurement at pH 7 alone. The soil-water partition coefficient is converted to a K_{oc} from the lowest non-sand K_d by multiplying by 0:0116. This is the organic carbon content in the A horizon of the Loring silt loam, the soil in the scenario that GENEEC uses internally. The EEC's do not reflect the concentration of any degradates. The version of GENEEC used for the calculations was GENEEC version 2 for Windows dated March 11, 1996. Table 2 contains the dietary equivalents for the drinking water values for US adults and children. The US adult value is based on the water consumption and self reported body-weights in the USDA 1977-1978 Food Survey. For the whole US population this value is 22.6 g-H_2O kg^{-1} d^{-1}. This value is identical to the value for the whole US population in Ershow and Cantor, 1989. The value for children is 50 g-H_2O kg^{-1} d^{-1} which is based on a 20 kg child drinking 1 L of water a day.

Calculating Risks using Drinking Water Exposure Estimates

For estimating chronic risk, the chronic dietary (other than drinking water) exposure in mg kg^{-1} d^{-1} can be added to the chronic drinking water exposure (in mg kg^{-1} d^{-1}) to estimate the total chronic dietary exposure. This value can then be used to estimate the chronic risk, either as a per cent of the RfD or to estimate the cancer risk. The process is somewhat more complicated for acute risk. Ideally, a probabilistic assessment that accounts for the likelihood that a person could receive elevated levels from different sources would be done. However, this kind of assessment is too time consuming for use at the screening level. However, in most cases, the acute risk is the result of exposure from a single highly contaminated source, so we can use an upper-bound estimate of the

exposure from single sources plus the background to estimate the acute risk. The chronic exposure due to sources other than the acute source is a suitable estimate of the background. Therefore we can use the larger of the following two values to estimate the acute dietary exposure: the acute water plus the dietary (other than water) background. or the acute dietary plus the chronic water. This value can then be used to calculate the Margin of Exposure as has been done in the past with just the acute dietary exposure with consideration of drinking water .

Table 1. GENEEC Input Parameters.	
Chemical	Vinclozolin
PC Code	113201
Solubility	2.6 mg L^{-1}
Hydrolysis	$T_{1/2}$ = 1.15 d; k = 6.03 x 10^{-1} d^{-1} (estimated from all hydrolysis data)
Photolysis	$T_{1/2}$ = 27.2 d; k = 2.55 x 10^{-2} d^{-1}
Aerobic Soil Metabolism	$T_{1/2}$ = 1056 d; 3 x a single value
Anaerobic Soil Metabolism	$T_{1/2}$ = 52.8 d; k = 1.31 x 10^{-2} d^{-1}, 3 times a single value
Anaerobic Aquatic Metabolism	402 d; k = 1.72 x 10^{-3} d^{-1}, 3 times a single value
Soil Water Partitioning	293 L kg-OC^{-1}; Kd converted K_{oc} by dividing by 0.0116
Identified Environmental Degradates	N-(3,5-dichlorophenyl) carbamic acid (1-carboxyl-1-methyl)-2-propenyl ester 3,5-dichloroaniline N-(3,5-dichlorophenyl)-2-hydroxy-2-methyl-3-butenoic acid amide
Source and Quality	EFGWB One-Liner & Mastradone, 1995
Prepared By	R. David Jones
Date	January 14, 1997
Crop	snap beans
Application Rate	0.5 lb $acre^{-1}$
Number Of Applications	2
Minimum Application Interval	7 d
Application Method	ground spray
Source	Ronilan DF Fungicide label with amendment
Date	February 20, 1997
Prepared By	R. David Jones

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Table 2. Body-weight based exposure values for surface-water-source drinking water containing vinclozolin.		
	Acute (mg kg^{-1} d^{-1})	Chronic (mg kg^{-1} d^{-1})
Adult	6.1×10^{-4}	2.4×10^{-5}
Child	1.4×10^{-3}	5.3×10^{-5}

Literature Cited

Ershow, Abby. G. and Kenneth P. Cantor. May, 1989. *Total Water and Tapwater Intake in the United States Population-Based Estimates of Quantities and Sources.* National Cancer Institute. Bethesda, MD.

Mastradone, Paul J. 1995. *EFGWB Review of Vinclozolin.* Memorandum to Bruce Sidwell/Mark Wilhite and Connie Welch dated July 1, 1995. D165556, D172180, D172184, D172187, D180848, D182128, D183906, D189301, D190221, D193639, D197666, D200149, D204484, D211115, D211724.

cc: EEC file
Arnet Jones

Attachment IV

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

FEB 21 1997

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

SUBJECT: Decision Meeting About Vinclozolin's Uncertainty Factors for Development Toxicity.

FROM: William L. Burnam, Chief
Science Analysis Branch

TO: Mike Metzner, Chief
Risk Characterization and Analysis Branch

On January 23, 1997, a meeting was held to discuss the pros and cons of assigning extra (greater then 100) uncertainty factors to the developmental toxicity endpoint of 3 mg/kg for vinclozolin. Those attending were as follows: Karl Baetcke, Karen Whitby, Sue Makris, Jim Rowe, Dave Anderson, Roger Gardner, Jeff Herdon, Kathryn Boyle and myself.

The unanimous conclusion was that an uncertainty factor of greater than 100 was not needed for the following reasons:

1. Vinclozolin has an adequate and extensive toxicity data base including mechanistic data.

2. Mechanistic data (androgen receptor inhibition) showing that vinclozolin probably results in analogous developmental effects in the rat and human.

3. There are probably only minor differences in kinetics and metabolism of vinclozolin between rats and humans.

4. Postnatal studies show effects in parents and offsprings at similar dose levels, although, the effects in offsprings are more severe.

5. The 3 mg/kg/day NOEL for decreased anogenital distance (AGD) as a measure of developmental effects is a very sensitive measure of decreased androgenization of the fetus/offspring.

6. The decreased AGD has only been seen in rat studies. Neither the rabbit nor the mouse developmental toxicity studies show obvious antiandrogen related effects.

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7. The 3 mg/kg/day endpoint may be overprotective since the next higher dose level (6 mg/kg/day) was not statistically significantly different from the control. Based on additional analysis by SAB statisticians, the NOEL may be as high as 12 mg/kg/day.

Based on the above considerations (details found in various vinclozolin supporting memos and presentations to the FIFRA Science Advisory Panel), additional uncertainty factors beyond the usual 100 X were not considered appropriate when used with the developmental toxicity endpoint of 3 mg/kg/day.

cc: Stephanie Irene
Karl Baetcke
Karen Whitby
Sue Makris
Jim Rowe
Dave Anderson
Roger Gardner
Jeff Herdon
Kathryn Boyle