

US EPA ARCHIVE DOCUMENT

(7-13-99)

DATA EVALUATION RECORD

CGA-153433

STUDY 1c

CHEM Clopidogrel-mexyl §163-1  
CAS No. 88349-88-6  
FORMULATION--00--ACTIVE INGREDIENT

STUDY ID 88888803

Hill, A. D. 1994. CGA-153433: Adsorption/desorption in three soils. Laboratory Study No.: HE 380/220. Novartis Study No.: 868-99. Unpublished study performed by Hazleton Europe, North Yorkshire, ENGLAND; and submitted by Novartis Crop Protection, Inc., Greensboro, NC.

DIRECT REVIEW TIME = 26 Hours

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## CONCLUSIONS

### Mobility - Leaching & Adsorption/Desorption

1. This <sup>Supplemental</sup> study ~~may not~~ be scientifically valid and ~~may not~~ provide useful information on the soil mobility (batch equilibrium) of the cloquintocet-mexyl degradate CGA-153433 in three soils. Material balances were not determined for the samples used in the definitive study.
2. This study does not meet Subdivision N Guidelines for the partial fulfillment of EPA data requirements on soil mobility (batch equilibrium) for the following reasons:
  - (i) material balances were not determined for samples utilized in the definitive study;
  - (ii) only three soils were utilized, all of which were foreign; and
  - (iii) none of the soils had an organic matter content of <1%.
  - (iv) Analytical Method Limits of detection & quantitation <sup>are</sup> too high.
3. Nonradiolabeled CGA-153433, at nominal concentrations of 5, 10, 25 and 50 ppm, was studied in loamy sand and two silt loam soil:solution slurries that were equilibrated for seven hours at  $20 \pm 1^\circ\text{C}$ . Freundlich  $K_{\text{ads}}$  values were 21.8 for the loamy sand soil (1.3% o.m.), 24.9 for the Les Evouettes silt loam soil, and 55.4 for the Vetroz silt loam soil (7.5% o.m.); corresponding  $K_{\text{oc}}$  values were 2870, 1186 and 1261 mL/g. Respective  $1/N$  values were 0.76, 0.73 and 0.80 for adsorption. Freundlich  $K_{\text{des}}$  values determined after a single 7-hour desorption period were 26.4 for the loamy sand soil, 27.5 for the Les Evouettes silt loam soil, and 67.2 for the Vetroz silt loam soil; corresponding  $K_{\text{oc}}$  values were 3474, 1309 and 1531 mL/g. Respective  $1/N$  values were 0.75, 0.72 and 0.79 for desorption. The reviewer-calculated coefficient of determination ( $r^2$ ) values for the relationships  $K_{\text{ads}}$  vs. pH,  $K_{\text{ads}}$  vs. organic matter, and  $K_{\text{ads}}$  vs. clay content were 0.011, 0.92 and 0.84, respectively.

## METHODOLOGY

In a preliminary study of the adsorption of nonradiolabeled CGA-153433 to loamy sand and two silt loam soils, an equilibration period of seven hours was chosen for all three soils for both the adsorption and desorption phases (p. 22); data were not reported. Based on the results of a preliminary study, a soil:solution ratio of (1:2, w:v) was chosen; data were not reported.

For the adsorption phase of the definitive study, aliquots (35 mL) of 0.01 M  $\text{CaCl}_2$  solution were added to polyallomer centrifuge bottles containing samples (20 g) of sieved (2 mm) Collombey loamy sand, Vetroz silt loam and Les Evouettes silt loam soils (Table

6.1, p. 36) and the soil:solution slurries were pre-equilibrated by shaking for 24 hours (p. 22). The pre-equilibrated slurries were treated with nonradiolabeled CGA-153433 {5-chloro-quinolin-8-yloxy)-acetic acid; chemical purity 99%; p. 20}, dissolved in methanol and 0.01 M CaCl<sub>2</sub> solution (5 mL), at nominal concentrations of 5, 10, 25 and 50 ppm. Duplicate samples were prepared for each soil type/treatment rate combination; two additional samples of each soil treated at 50 ppm were prepared for mass balance determinations (p. 23; see Comment #1). The soil:solution (1:2, w:v) slurries were equilibrated by shaking for seven hours at 20 ± 1 °C. Following the adsorption equilibration period, the soil:solution slurries were centrifuged and the supernatant was decanted. Aliquots of each supernatant were analyzed by HPLC (Nucleosil 5 C18 column) using an isocratic mobile phase of 0.1 M ammonium acetate:acetonitrile:acetic acid (75:25:0.2, v:v:v) with UV (228 nm) detection (p. 25).

For the desorption phase of the definitive study, an aliquot (40 mL) of pesticide-free 0.01 M CaCl<sub>2</sub> solution was added to each of the soil pellets from the adsorption phase of the definitive study (p. 23). The soil:solution (1:2, w:v) slurries were equilibrated by shaking for seven hours at 20 ± 1 °C. The soil:solution slurries were centrifuged and the supernatant was decanted. Aliquots of the supernatant were analyzed by HPLC as previously described. The desorption was repeated as previously described

#### DATA SUMMARY

Nonradiolabeled CGA-153433 (chemical purity 99%), at nominal concentrations of 5, 10, 25 and 50 ppm, was studied in loamy sand and two silt loam soil:solution slurries that were equilibrated for seven hours at 20 ± 1 °C. Freundlich  $K_{ads}$  values were 21.8 for the loamy sand soil (1.3% o.m.), 24.9 for the Les Evouettes silt loam soil, and 55.4 for the Vetroz silt loam soil (7.5% o.m.; Table 6.10, p. 45); corresponding  $K_{oc}$  values were 2870, 1186 and 1261 mL/g (Table 6.11, p. 46). Respective 1/N values were 0.76, 0.73 and 0.80 for adsorption. The reviewer-calculated coefficient of determination ( $r^2$ ) values for the relationships  $K_{ads}$  vs. pH,  $K_{ads}$  vs. organic matter, and  $K_{ads}$  vs. clay content were 0.011, 0.92 and 0.84, respectively. Freundlich  $K_{des}$  values determined after a single 7-hour desorption period were 26.4 for the loamy sand soil, 27.5 for the Les Evouettes silt loam soil, and 67.2 for the Vetroz silt loam soil; corresponding  $K_{oc}$  values were 3474, 1309 and 1531 mL/g. Respective 1/N values were 0.75, 0.72 and 0.79 for desorption.

During the 7-hour equilibration period, 87.0-93.4% of the nominal concentration was adsorbed to the loamy sand soil (for all replicates across all application levels; Table 6.8, p. 43), 87.7-94.2% of the nominal was adsorbed to the Les Evouettes silt loam soil (Table 6.9, p. 44), and 95.7-97.6% of the nominal was adsorbed to the Vetroz silt loam soil (Table 6.7, p. 42). Following the first 7-hour desorption period, 4.4-9.0%, 4.1-9.3% and 1.3-2.8% of the previously adsorbed test compound was desorbed from the loamy sand, Les Evouettes silt loam and Vetroz silt loam soils, respectively; after the second 7-hour

desorption period, 5.2-8.4%, 3.8-7.8% and 1.2-2.8% of the previously adsorbed compound was desorbed, respectively.

The stability of the test compound in the soil:solution slurries following adsorption was confirmed by HPLC analysis of the soil extracts from the additional sets of duplicate samples treated at 50 ppm (p. 17).

Material balances were not determined for samples utilized in the definitive study, but were determined for the additional samples of each soil which were treated at 50 ppm. Material balances (reviewer-calculated mean of two replicates) following the adsorption period were 93.2%, 90.8% and 97.6% of the nominal application for the loamy sand, Les Evouettes silt loam and Vetroz silt loam soils, respectively (Table 6.13, p. 48).

#### COMMENTS

1. Material balances were not determined for samples utilized in the definitive study, but were determined for separate duplicate samples of each soil treated at 50 ppm (p. 23). Material balances for all samples utilized in the definitive study are needed to assess the validity of the study. Because the compound was determined to be immobile in each of the three soils studied, it is important that complete material balance information be reported in order to confirm that the parent material was adequately recovered and that it was not adsorbed to the sides of the test vessels during the study. The reviewer notes that the test vessels were washed with methanol and the rinsate analyzed for parent compound; results indicated that the parent did not adsorb to the test vessels. However, this procedure was only conducted following the second desorption equilibration period. Additionally, the reviewer notes that the limits of detection and quantitation were relatively high for the analysis of soil samples, at 2 ppm and 5 ppm, respectively; the <sup>too</sup> lowest treatment rate utilized in the study was 5 ppm.
2. Only three soils were used in the study, all of which were foreign. Subdivision N Guidelines require that mobility studies be conducted using at least four soils. EPA prefers the use of domestic soils in mobility studies (U.S. EPA Rejection Rate Analysis, EPA 738-R-93-010, September 1993). However, the agency will accept non-domestic/European soils for two of the four soils required if and only if the soils are characterized according to the USDA system. The reviewer could not confirm that the soils utilized in this study were characterized using the USDA system.
3. None of the soils had an organic matter content of <1% (Table 6.1, p. 36). Subdivision N Guidelines require that at least one soil used in mobility studies have an organic matter content of <1%.
4. The test compound CGA-153433 is a metabolite of cloqiontocet-mexyl (CGA 185072)

which is a safener used with the herbicide clodinafop-propargyl.

5. The  $1/N$  values for all three soils were  $<0.9$  for both the adsorption and desorption phases of the study; therefore, the Freundlich isotherm may not accurately depict the adsorption of the parent compound in these soils across all concentrations (Table 6.10, p. 45).
6. It was not reported whether the test compound was stable during the adsorption and desorption phases of the definitive study. Supernatants were analyzed by HPLC; however, residue data were not reported. The reviewer notes, however, that the stability of the test compound following adsorption was determined using the soil extracts from the additional sets of duplicate samples treated at 50 ppm. Results indicated that the compound was stable in the soil extracts (p. 17); data were not reported.
7. The study author stated that, following the second desorption equilibration period, the soil was removed from the test vessels and the bottles were rinsed by shaking with methanol (p. 23). The rinsate was analyzed by HPLC to determine the adsorbance of the test compound to the bottles. The study author stated that the analyses of the methanol rinsate indicated that no test substance had been adsorbed to the walls of the centrifuge bottles (p. 32).
8. Method detection limits were reported only on sample HPCL chromatographs. The limits of detection in water and soil were 0.05 ppm and 2 ppm, respectively; the limits of quantitation in water and soil were 0.1 ppm and 5 ppm, respectively (pp. 51-56).
9. The study author did not state whether one of the soils is the same soil utilized in the aerobic soil metabolism study. The reviewer did not have access to an aerobic soil metabolism study.
10. The percentage organic matter for each soil was calculated by the reviewer by multiplying the percentage organic carbon reported in Table 6.1 (p. 36) by 1.7.
11. The aqueous solubility of CGA-153433 was reported as 10.2 g/L at pH 5.2 (p. 20).

NO MRID AS OF NOW

VOLUME \_\_\_\_ OF \_\_\_\_ OF SUBMISSION

CGA-153433: FINAL REPORT  
(Metabolite of CGA-185072)

will submit  
AND OBTAIN

TITLE

MRID #  
John Jordan  
4/28/99

CGA-153433: ADSORPTION/DESORPTION IN THREE SOILS

DATA REQUIREMENT

The EC Directive 91/414/EEC Active Substances, Section 7.1.2 (Draft July 1993), OECD  
Guideline 106 for the testing of Chemicals (May 1981)

AUTHOR

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COMPLETION DATE

April 4, 1994

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LABORATORY STUDY IDENTIFICATION

Novartis Number 868-99  
Study Number: HE 380/220  
Study Report Number: 380/220-1015

SUBMITTER/SPONSOR

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VOLUME 1 OF 1 OF STUDY

PAGE 1 OF 85

6

CLOQUIONTOCET MEXYL

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\_\_\_\_\_ Identity of product impurities.

\_\_\_\_\_ Description of the product manufacturing process.

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