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

JUN 17 1991

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM (Confidential)

Subject: Paclobutrazol Product Chemistry: Analytical Methods to Determine Impurities. Chemical 125601. I. D. No. 10182-77. DP Barcode D162518. MRID No. 417973-01. CBRS No. 7819.

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Background

In response to a 06/87 DCI, ICI Americas, Inc. previously submitted manufacturing data for technical (2RS, 3RS)-1-(4-chlorophenyl)-4,4-dimethyl-2-(1H-1,2,4-triazol-1-yl) pentan-3-ol, or paclobutrazol. The purpose of the DCI is to acquire information on the potential for formation of halogenated dibenzo-p-dioxin or dibenzofuran contaminants during certain manufacturing processes. The data were reviewed and it was concluded that formation of polyhalogenated dioxin and/or dibenzofuran impurities is unlikely under the manufacturing conditions described (02/26/90 Memorandum, S. Funk, DEB No. 6091). It was also concluded that precision and accuracy data were required for the methods used to certify the concentration limits of impurities. The registrant was requested to submit details of the analytical methods, proof of a detection limit of 0.1% for each impurity, actual sample chromatograms, and accuracy and precision data for the method(s).

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MANUFACTURING PROCESS INFORMATION IS NOT INCLUDED

Discussion

The registrant has responded with a document entitled "Paclobutrazol: Standard Official Method," received 02/27/91. Method SOM 4201/06/90B is utilized to determine paclobutrazol and all organic impurities except [redacted] The method is capillary GC with a FID, as opposed to a HPLC procedure outlined in the original submission. The column is DB17 (15 m X 0.25 mm X 0.25 micron), and split injection mode is used. The oven is programmed from 170 deg C to 210 deg. C at 20 deg. C/minute, held at 210 deg. C for 5 minutes, and programmed at 30 deg. C/min. to a final temperature of 280 deg. C. The final peak elutes at about 11.3 minutes. N-docosane (0.25%) is used as an internal standard.

Precision and accuracy results are presented for the analysis of three weighings of a technical standard of known composition. Five determinations were made on each of the three samples. Results are as follows:

Compound	Actual Conc. (% w/w)	Accuracy (% recovery)	Precision (% RSD)
paclobutrazol	91.00	99.8	0.32

Satisfactory accuracy and precision have been demonstrated at levels typical of concentrations in the technical product. Several chromatograms are included. Peak shape and resolution are adequate.

The registrant attempted a demonstration of the linearity of detector response for the active ingredient and impurities in the

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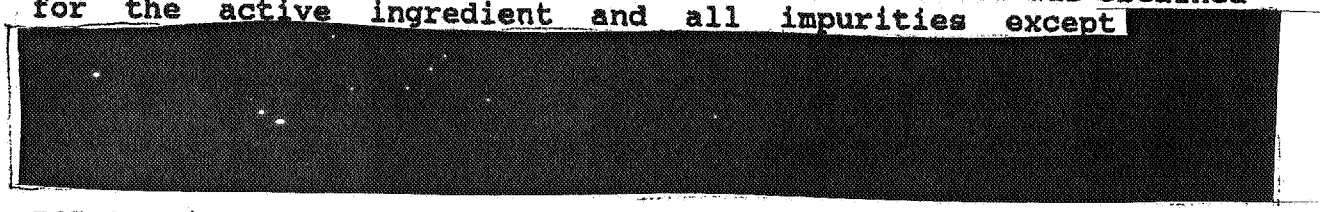
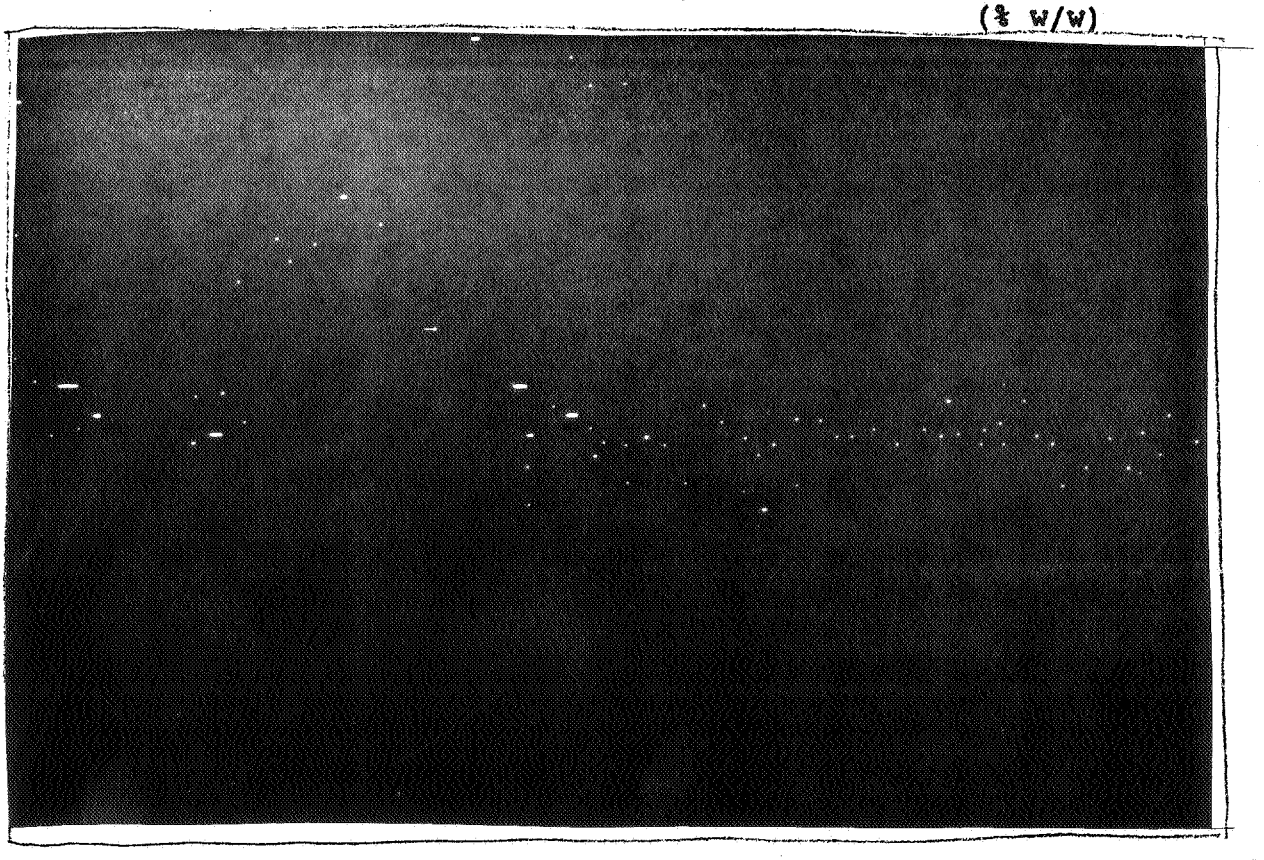
concentration range found in the technical product. Four concentrations, 0.25X, 0.50X, 1X, and 2X the anticipated concentrations, were analyzed. However, the registrant varied the internal standard in the same fashion. All relative concentrations remained the same. The internal standard concentration should have been constant, as would be the case with the analysis of routine samples. Chromatograms, linearity plots, and correlation coefficients are provided. A value of at least 0.9999 was obtained for the active ingredient and all impurities except



ICI Americas, Inc. calculated limits of detection (lod) for each impurity based on peak height of each impurity peak in a standard and the baseline noise. The lod was defined as 3X the baseline noise. The calculations are presented, and the following limits of detection were determined:

Impurity	Concentration Measured (% w/w)	Limit of Detection (% w/w)



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[1] Calculated based on the limit of detection of the active ingredient and the relative responses of the impurity and the active.

The GC method for the determination of the [redacted] impurity and the associated validation data were also presented.

Conclusion

MANUFACTURING PROCESS INFORMATION IS NOT INCLUDED

The registrant has submitted the required analytical method and has demonstrated that the method has sufficient accuracy, precision, and sensitivity to determine the impurities at the certified levels of the CSF. The registrant did not properly demonstrate the linearity of the method in the concentration ranges of interest. However, capillary column/FID is anticipated to have a wide (at least 10^2) linear range.

Recommendation

The data gap is resolved. No further action is needed.

cc: RF, Dioxin SF, , S. Funk, C. Furlow (PIB, FOD).

RDI:A. Rathman:06/12/91:E. Zager:06/12/91:

H7509C:CBRS:S.Funk:557-1430:CM#2:RM803-A:SF(DIOX.105):06/07/91.