



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY


WASHINGTON, D.C. 20460



OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

May 6, 2002

MEMORANDUM

SUBJECT: Chlorpropham (CIPC) [018301], Response to Registrant's Letter dated March 13, 2002 Regarding Agency Review of Residue Study Reports. DP Barcode D281664 (No MRID).

From: Danette Drew, Chemist 
Reregistration Branch 3
Health Effects Division [7509C]

Through: Steve Knizner, Branch Chief 
Catherine Eiden, Branch Senior Scientist 
Reregistration Branch 3
Health Effects Division [7509C]

To: Gary Mullins
Reregistration Branch 3
Special Review and Reregistration Division [7508C]

Executive Summary

Special Review and Reregistration Division (SRRD) has requested that the Health Effects Division (HED) address a letter dated March 13, 2002 (including an enclosed letter dated March 12, 2002), *Response to Agency Reviews of Pin Nip Residue Study Reports*, submitted on behalf of Pin Nip, Inc. The letter is a response to HED's review of two previously submitted studies: *Magnitude of the Residue of Chlorpropham on Potato Skin and Potato Pulp Following Treatment with Chlorpropham Emulsifiable Concentrate Form* (MRID44736001; D260114, D. Drew, 12/17/01) and *Magnitude of the Residue of Chlorpropham on Potato Skin After Post-Harvest Fumigation* (MRID 45426101; D276548, D. Drew, 1/7/02). HED has responded to Pin Nip's comments on a point-by-point basis as outlined in this memorandum. The Pin Nip comments have been abbreviated by the reviewer (see full comments in the attached letter, 3/13/02).

Magnitude of the Residue of Chlorpropham on Potato Skin and Potato Pulp Following Treatment with Chlorpropham Emulsifiable Concentrate Form (MRID 44736001)

1. Review Conclusion: The analytical method was not validated concurrently with the residue analysis.

Pin Nip Comment: The analytical method used in this study is essentially identical to the HPLC/UV method (MRID 44397101) that HED had deemed acceptable for data collection purposes. This method had also undergone an additional GLP-compliant method validation five months prior to the initiation of the residue study (Pin Nip Study No. 97-001). Therefore, the analytical method had been shown to be valid and appropriate for the measurement of chlorpropham residue levels and had been validated concurrently with the study's residue analysis.

HED Response: Although the HPLC/UV method used in the potato residue study has been deemed acceptable for data collection purposes (D185464, 4/16/93 and D193416, 8/11/93, J. Abbotts) and has undergone previous successful method validation, there is no evidence that the method was also validated *concurrently* with the residue study. Concurrent method validation should be performed every time a residue study is performed, along with that study. This is done not so much to determine the method acceptability, but to ensure that instrument or other conditions, extraction technique, and operator technique have not changed significantly over time and that the method LOQ is still obtainable at the time the samples are analyzed. The concurrent method validation samples provide assurance that the method is performing adequately on the specific day that field trial samples are being analyzed. The OPPTS Test Guideline 860.1500 (h)(3)(vi)(E) states that "Method recovery validation studies should be run *concurrently with the residue analyses of crop field trial samples from each individual field trial* in order to provide information on the recovery levels of the test compounds from the test substrates at various fortification levels using the residue analytical methods, and to establish a validated limit of quantitation."

Unless there are data showing concurrent validation of the study, HED reiterates that for MRID 44736001 "the submitted residue data for potato peels and pulp are not adequate because the method used for analysis was not validated concurrently with the residue analyses".

2. Review Conclusion: Sufficient details of chlorpropham applications were not provided.

Pin Nip Comment: This study measures residues resulting from the application of an emulsifiable concentrate (EC) chlorpropham formulation to potatoes previously maintained in storage. Although the study noted that the potatoes had previously been treated with an aerosol chlorpropham product while in storage at a commercial storage facility, the report did not state application rates used in the aerosol treatments.

The amount of chlorpropham previously applied to the studies is not relevant to the study results. The study measures residues resulting from EC applications. The study took into account the background levels of CIPC on the potatoes by determining residues on control (non- EC treated) samples at each interval and by determining residues in EC treated and non-EC treated samples at zero time (Note: all samples had been previously treated with aerosol fogger).

The Data Call-In from the Reregistration Standard, which required residue studies for both aerosol and EC formulations, expressly permitted registrants to conduct separate residue tests for each type of product. EC products are used only after potatoes are maintained in storage. Therefore, potatoes receiving EC treatments would have been previously treated with an aerosol product. This study took into account residues from prior treatments and therefore is valid.

HED Response: Although the study does measure chlorpropham on potatoes prior to and after EC treatments, and the proposed tolerance is not exceeded in either case, there is no way of knowing if the previous aerosol application was applied at the *maximum* application rate and *minimum* retreatment interval that would result in the highest possible residue [see OPPTS Guideline 860.1500 (b) "crop field trials are conducted to determine the magnitude of the pesticide residue in or on raw agricultural commodities (RACs) and to reflect pesticide use patterns that could lead to the highest possible residues. The pesticide must be applied at known application rates and in a manner similar to the use directions intended for the pesticide"]].

If the potatoes had been previously treated at a level lower than the maximum rate, the resulting residues from this study are likely lower than those that would result from maximum treatment rates. In this case, HED could not say that the tolerance for chlorpropham on potatoes would definitely *not* be exceeded after application of EC to potatoes that had been previously treated in storage. If the potatoes in the study were in fact aerosol treated in storage at the maximum rate and minimum interval, and then treated with the EC, then HED could confidently state that the chlorpropham tolerance would not be exceeded as a result of potatoes being treated by both aerosol and EC formulations.

However, potatoes treated by EC alone, with no prior aerosol treatment, are not likely to have residues above the proposed tolerance.

HED and SRRD were unable to locate the Data Call-In, referenced by Pin Nip, with information regarding the residue data requirements for the EC and aerosol formulations (not in the DCIs issues 4/1/94 and 12/3/96). If the registrant has a copy of that Data Call -In, or can give a more specific reference, HED would appreciate a copy.

3. Review Conclusion: The values for chlorpropham residues in/on peel and pulp were reported in terms of whole potato weight rather than in terms of the weight of each fraction.

Pin Nip Comment: Values of chlorpropham were reported in both terms of whole potato weight and in terms of the weight of each fraction. The final report lists residues in potato skin as ug chlorpropham per g of skin. Potato pulp residues were also reported in terms of ug/g.

HED Response: The registrant is correct. Residue for potato skin and for pulp were reported separately in terms of each fraction weight. The separate fractions were also reported in terms of the whole potato weight. The residues from each fraction were combined mathematically to calculate whole potato residue. While it is preferable to perform residue analyses on the *whole* raw agricultural commodity, using the sum of fractions as whole potato weight will not be considered a deficiency for this study.

It is recommended that, in the future, any residue analyses be performed on whole potatoes since tolerances are established for residues on the whole raw agricultural commodity as it moves through interstate commerce [see OPPTS Guideline 860.1500(c)(2) "the sample should not be brushed, stripped, trimmed, or washed except to the extent that these are commercial practices prior to shipment, or to the extent allowable in 40 CFR180.1 (j)]. Residue data on commodities that have been trimmed, washed or otherwise prepared prior to analysis, while not necessarily suitable for establishing tolerances, may be considered for use in dietary risk assessments.

Magnitude of the Residue of Chlorpropham on Potato Skin After Post-Harvest Fumigation (MRID 45426101)

1. Review Conclusion: The residue data are not adequate because the method used for analysis was not validated concurrently with the residue analysis.

Pin Nip Comment: Same as Pin Nip Response for MRID 44736001 Review Conclusion # 1 above.

HED Response: Same as HED response for MRID 44736001 Review Conclusion # 1 above. Unless there are data showing concurrent validation of the study, HED reiterates that for MRID 45426101 "the submitted residue data for potato peels and pulp are not adequate because the method used for analysis was not validated concurrently with the residue analyses".

2. Review conclusion: Information pertaining to storage conditions was not provided.

Pin Nip Comment: The study report described the storage conditions by stating that the samples were refrigerated until processed and that all samples were processed within 10 days of collection. The refrigerator temperature was measured daily and recorded on a log. Accompanying this letter are three pages from the log, showing the daily temperatures of the refrigerator during the conduct of the study.

HED Response: HED has reviewed the submitted refrigerator log pages and has determined that the deficiency pertaining to storage conditions has been fulfilled.

cc: RF, List A file, D.Drew, Gary Mullins (SRRD), Cynthia Giles-Parker (RD).
RDI: S. Knizner 5/8/02 ; C Eiden 5/8/02
D.Drew: CM2, Rm 821E, 305-6028