

US EPA ARCHIVE DOCUMENT

R.F.



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

OCT 16 1991

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Chlorpropham Product and Residue Chemistry
Reregistration Standard Updates. CBRS No. 7672. DP
BARCODE D161067. No MRID.

FROM: E. Zager, Chief *Debra Edwards, for*
Chemistry Branch II: Reregistration Support
Health Effects Division (H7509C)

TO: Lois Rossi, Chief
Reregistration Branch
Special Review and Reregistration Division (H7508C)

and

William Burnam, Ph.D., Acting Chief
Science Analysis and Coordination Branch
Health Effects Division (H7509C)

Attached are the updates to the Product and Residue Chemistry Chapters of the Chlorpropham Reregistration Standard. These updates were prepared by Acurex Corporation under supervision of CBRS, HED. They have undergone secondary review in the branch and have been revised to reflect Agency policies.

A revised residue chemistry data requirement table is included. Since the product chemistry data requirements stated in the August, 1987 Product Chemistry Chapter remain unchanged, revised product chemistry data requirements tables are not included. No new data requirements for reregistration of Chlorpropham were identified in these updates.

If you need additional input please advise.

Attachment 1: Chlorpropham Product Chemistry Reregistration Standard Update. (This document does not contain any CBI.)

Attachment 2: Chlorpropham Residue Chemistry Reregistration Standard Update.

cc (With Attachments 1 and 2): P. Deschamp, Chlorpropham Reregistration Standard File, Chlorpropham Subject File, C. Furlow (PIB/FOD), and Acurex.

cc (With Attachments 1 and 2): Circulation (7).

ATTACHMENT 1

CHLORPROPHAM
(Chemical Code 018301)

TASK 3

**Reregistration Standard
Update**

Product Chemistry

July 19, 1991

Contract No. 68-DO-0142

Submitted to:

U.S. Environmental Protection Agency
Arlington, VA 22202

Submitted by:

Acurex Corporation
Environmental Systems Division
4915 Prospectus Drive
P.O. Box 13109
Research Triangle Park, NC 27709

CHLORPROPHAM

Chemical Code 018301

REREGISTRATION STANDARD UPDATE

PRODUCT CHEMISTRY

TASK 3

INTRODUCTION

A Product Search Listing conducted on March 14, 1991, identified two 98% technical (T) products of chlorpropham registered by Aceto Agricultural Chemicals Corporation (EPA Reg. Nos. 2749-102 and 2749-117).

The Guidance Document dated December, 1987 requires additional generic and product-specific chemistry data for the chlorpropham manufacturing-use products. Aceto Agricultural Chemicals Corp. has not submitted product chemistry data for either of the 98% technicals (EPA Reg. Nos. 2749-102 and 2749-117). All data pertaining to these topics are required for these products.

Corresponding to each of the Topical Discussions listed below are the Guideline Reference Numbers from "Pesticide Assessment Guidelines-Subdivision D-Product Chemistry," referred to in Title 40 of the Code of Federal Regulations (40 CFR), Part 158, "Data Requirements for Registration," Subpart C, "Product Chemistry Data Requirements." These regulations and guidelines explain the minimum data that the Agency needs to adequately assess the product chemistry of chlorpropham.

Guideline Reference No.
from 40 CFR §158.155-190

Product Composition and Manufacture	61-(1-3)
Analysis and Certification of Product Ingredients	62-(1-3)
Physical and Chemical Characteristics	63-(2-20)

SUMMARY

The following product chemistry data remain outstanding:

- o All product chemistry data remain outstanding for the Aceto Agricultural Chemicals Corp. 98% technicals (EPA Reg. Nos. 2749-102 and 2749-117).

ATTACHMENT 2

**CHLORPROPHAM
(Chemical Code 018301)**

TASK 3

**Reregistration Standard
Update**

Residue Chemistry

July 19, 1991

Contract No. 68-DO-0142

Submitted to:

U.S. Environmental Protection Agency
Arlington, VA 22202

Submitted by:

Acurex Corporation
Environmental Systems Division
4915 Prospectus Drive
P.O. Box 13109
Research Triangle Park, NC 27709

CHLORPROPHAM

(Chemical Code 018301)

REREGISTRATION STANDARD UPDATE

RESIDUE CHEMISTRY

Task - 3

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CHLORPROPHAM

(Chemical Code 018301)

REREGISTRATION STANDARD UPDATE

RESIDUE CHEMISTRY

Task - 3

INTRODUCTION

Chlorpropham is the common name for isopropyl 3-chlorocarbanilate (CIPC), a plant growth regulator registered for postharvest use on potatoes (SPO5 Site Listing printout dated March 14, 1991); products registered for this use include the 25%, 36%, and 46.5% emulsifiable concentrate (EC), the 46% soluble concentrate/liquid (SC/L), and the 49.65% and 78.5% ready-to-use (RTU) formulations (PRD1 Product Listing dated March 14, 1991). In addition, the 36% EC formulation is registered for field use in VA on dormant spinach under EPA SLN No. VA910004 (parent label EPA Reg. No. 34704-613).

Permanent tolerances have been established for residues of chlorpropham and its metabolite 1-hydroxy-2-propyl-3-chlorocarbanilate (calculated as residues of chlorpropham) in or on potatoes (postharvest) and soybeans (40 CFR §180.181). Interim tolerances are in effect for residues of chlorpropham in or on alfalfa, alfalfa hay, beans (dry and succulent), blackberries, blueberries, carrots, clover, clover hay, cranberries, garlic, grass, grass hay, onions, peas (dry and succulent), raspberries, rice grain, safflower seed, spinach, sugar beet tops, sugar beet roots, tomatoes, and the eggs, milk, and meat, fat, and meat byproducts of cattle, goats, hogs, horses, poultry, and sheep (40 CFR §180.319).

Chlorpropham was the subject of a Residue Chemistry Chapter dated August 14, 1987, and a Guidance Document dated December, 1987. The Chlorpropham Guidance Document required data on plant and animal metabolism, storage stability, residue analytical methods, and magnitude of residues in plants; requirements for data depicting magnitude of residues in livestock and animal commodities were reserved, pending evaluation of the required metabolism data. The Guidance Document required data on the magnitude of residues in drinking and irrigation water, and nature and magnitude of residues in fish and shellfish, following aquatic use on cranberries. The Guidance Document also required specific data concerning possible residues of 3-chloroaniline, a probable mutagen and a metabolite of chlorpropham that was cited in the Chlorpropham Residue Chemistry Chapter to occur in several plant species.

In response to the Guidance Document, the registrants indicated the intent to voluntarily cancel all outdoor uses of chlorpropham on food and feed commodities, and requested a reevaluation of residue chemistry data requirements based on the remaining use of chlorpropham on stored potatoes (H. Fonouni, CBRS No. 6272, dated April 4, 1990). The

reviewer reevaluated the requirements and concluded that data are not required for those plant commodities affected by use cancellation, but that Guidance Document data requirements pertaining to potatoes (tuber metabolism, animal metabolism, residue analytical methods, storage stability, and magnitude of residues) remain in effect. The reviewer also concluded that because aquatic use of chlorpropham on cranberries has been canceled, data are no longer required for drinking and irrigation water, fish, and shellfish.

Subsequent to the cancellation of all uses except to potatoes following harvest, the USDA requested clarification of data required to support the field use of chlorpropham on carrots grown in all domestic regions and on spinach grown in all domestic regions except CA (P. Deschamp, CBRS No. 7803, dated April 9, 1991). The reviewer reevaluated the requirements and concluded that Guidance Document data requirements pertaining to carrots and spinach (animal metabolism, residue analytical methods, and storage stability), as well as data requirements pertaining to magnitude of residues as stated in CBRS No. 7803, must be fulfilled in order to support the indicated uses on carrots and spinach.

No residue chemistry data have been submitted in response to the Chlorpropham Guidance Document. The Chlorpropham Task Force requested a time extension for data submission; the Branch expressed no objection to this request (W. Smith, CBRS No. 7432, dated March 13, 1991). The proposed schedule for data submission is as follows: plant residue analytical methods and storage stability - July 15, 1991; plant metabolism - August 15, 1991; ruminant and poultry metabolism - December 15, 1991; animal residue analytical methods - January 15, 1992; magnitude of residues in animals - July 15, 1992; and magnitude of residues in potatoes - July 15, 1993.

SUMMARY

The following residue chemistry data requirements remain outstanding:

- o Data concerning nature of the residue in stored potato tubers.
- o Data concerning nature of the residue in ruminants and poultry.
- o Validated methodology for data collection and enforcement that can recover free and conjugated residues of concern, including 3-chloroaniline.
- o Storage stability data.
- o Data concerning magnitude of residues in or on spinach, and the raw and processed commodities of potatoes.

QUALITATIVE NATURE OF THE RESIDUE IN PLANTS

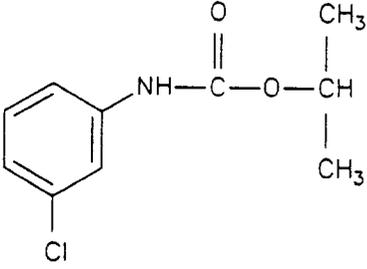
Conclusions:

The Chlorpropham Guidance Document dated December, 1987 required data depicting the metabolism of chlorpropham in stored potato tubers. No potato metabolism data have been submitted in response to the Guidance Document; however, the Chlorpropham Task Force indicated the intent to submit these data by August 15, 1991 (W. Smith, CBRS No. 7432, dated March 13, 1991). The requirements specified in the Guidance Document are reiterated below:

- o Data must be submitted depicting the uptake, distribution, and metabolism of ring-labeled [¹⁴C]chlorpropham in stored potatoes following postharvest application at a rate sufficiently high to permit complete ¹⁴C-residue characterization. Representative samples from the required metabolism studies must also be analyzed using accepted enforcement methods to ascertain that these methods will determine all possible metabolites of concern, including any bound/conjugated residues of concern.

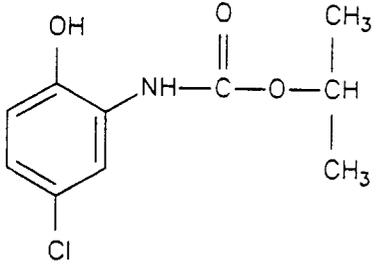
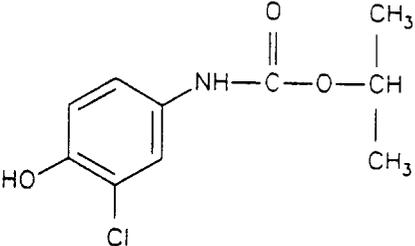
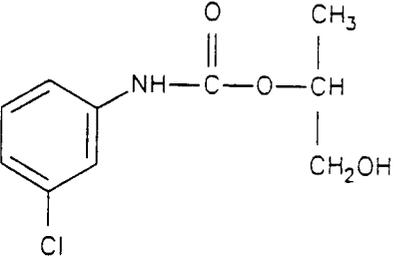
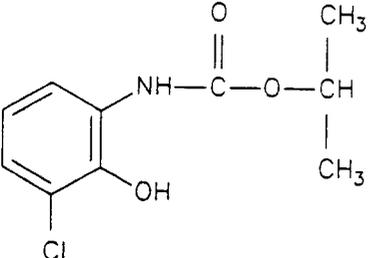
The Chlorpropham Residue Chemistry Chapter dated August 14, 1987 concluded that the nature of the residue in field-treated, growing plants is adequately understood. A summary of the known metabolites of chlorpropham in plants and animals, depicting molecular structures and listing substrates from which they were identified, is presented in Table 1 below. As indicated in the studies reviewed for the Residue Chemistry Chapter, the major residues of chlorpropham in plants are chlorpropham (I), 6-OH-CIPC (II), 4-OH-CIPC (III), isopropyl-OH-CIPC (IV), and 2-OH-CIPC (V). Conjugated residues occurred in both soluble and insoluble fractions of plant matrices.

Table 1. Known metabolites of chlorpropham (isopropyl 3-chlorocarbanilate) in plants and animals.

Code Number	Chemical Name	Chemical Structure	Found In
I	Isopropyl 3-chlorocarbanilate; Isopropyl m-chlorocarbanilate (Chlorpropham; CIPC)		soybeans

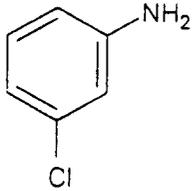
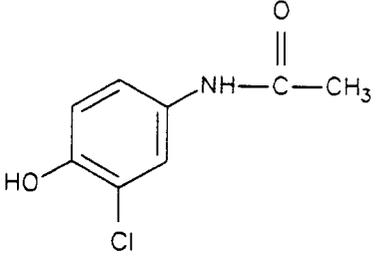
(Continued)

Table 1. Continued.

Code Number	Chemical Name	Chemical Structure	Found In
II	Isopropyl 3-chloro-6-hydroxy-carbanilate (6-OH-CIPC; I)		soybeans alfalfa orchard-grass turnips
III	Isopropyl 3-chloro-4-hydroxy-carbanilate (4-OH-CIPC; II)		soybeans alfalfa cucumbers orchard-grass cow's milk
IV	1-Hydroxy-2-propyl-3-chloro-carbanilate (Isopropyl-OH-CIPC; III)		soybeans orchard-grass turnips
V	Isopropyl 3-chloro-2-hydroxy-carbanilate (2-OH-CIPC; IV)		soybeans orchard-grass turnips

(Continued)

Table 1. Continued.

Code Number	Chemical Name	Chemical Structure	Found In
VI	3-Chloroaniline (Chloroaniline)		smartweed pigweed tomatoes parsnips
VII	3-Chloro-4-hydroxyacetanilide (4-OH-acetanilide)		cow's milk

References (used):

N/A.

Discussion of the data:

N/A.

QUALITATIVE NATURE OF THE RESIDUE IN ANIMALS

Conclusions:

The Chlorpropham Guidance Document dated December, 1987 required data depicting the metabolism of chlorpropham in ruminants and poultry. The Agency reevaluated these requirements, taking into account the voluntary cancellation of chlorpropham use on all commodities except potatoes following harvest, and concluded that metabolism data for animals are still required because culled potatoes are a livestock feed item (H. Fonouni, CBRS No. 6272, dated April 4, 1990). No animal metabolism data have been submitted in response to the Guidance Document; however, the Chlorpropham Task Force indicated the

intent to submit these data by December 15, 1991 (W. Smith, CBRS No. 7432, dated March 13, 1991). The requirements specified in the Guidance Document are reiterated below:

- o Metabolism studies must be submitted utilizing ruminants and poultry. Animals must be dosed for a minimum of 3 days with ring-labeled [¹⁴C]chlorpropham at a level sufficient to make identification and quantification of residues possible. Milk and eggs must be collected for analysis twice daily during the dosing period, and animals must be sacrificed within 24 hours after administration of the final dose. The distribution and identity of residues must be determined in milk, liver, kidney, muscle, and fat of ruminants, and in eggs, liver, kidney, muscle, and fat of poultry. Samples from the requested animal metabolism studies must also be analyzed using current enforcement methods to determine the usefulness of these methods for analysis of animal commodities. The enforcement method must be capable of determining all free and bound/conjugated residues of concern.

References (used):

N/A.

Discussion of the data:

N/A.

RESIDUE ANALYTICAL METHODS

Conclusions:

The metabolism of chlorpropham in harvested potato tubers and in livestock is not adequately understood. Following receipt of the requested metabolism data, additional requirements for analytical methodology may be mandated.

The Chlorpropham Residue Chemistry Chapter dated August 14, 1987 concluded that data collection and enforcement methodology should include pre-hydrolysis extraction steps in order to detect free and conjugated side-chain modified metabolites, such as isopropyl-OH-CIPC and 3-chloroaniline. The Chapter identified GLC methods submitted in PPG Report Nos. BTS-16129 and BR-18920. The Chlorpropham Guidance Document dated December, 1987 required the registrants to select specific method(s) for tolerance enforcement. In addition, the Guidance Document also specified that methods used for data collection, including methods specific for 3-chloroaniline, be tested with regard to their efficiency in extracting bound residues. To this end, it is recommended that methods be validated with weathered radioactive residues in conjunction with the required metabolism studies.

Following reevaluation of the Guidance Document requirements, CBRS reiterated the need for method validation using labeled weathered residues and stated that the methods used for data collection be suitable for enforcement purposes (H. Fonouni, CBRS No. 6272, dated April 4, 1990). We note that the Agency now requires that proposed enforcement methodology be validated by an independent laboratory prior to being submitted for Agency validation trials.

No analytical methodology data have been submitted in response to the requirements; however, the Chlorpropham Task Force has indicated the intent to submit data for potatoes by July 15, 1991 and data for animals by January 15, 1992 (W. Smith, CBRS No. 7432, dated March 13, 1991). The requirements specified in the Guidance Document and in CBRS No. 6272 are stated below:

- o The registrant must select the specific method(s) recommended for tolerance enforcement. The method must include a hydrolysis step at the tissue stage to release bound/conjugated residues. Spiking may not produce conjugates. Therefore, enforcement methods must be tested in conjunction with plant and animal metabolism studies. The efficiency of extraction of bound/conjugated residues of concern must be determined for any or all residue data collection methods the registrant has used or will use to support tolerances. Residues must be "weathered" and not simply spiked into samples prior to analysis. This may best be conducted in conjunction with plant and animal metabolism studies involving radiolabeled material. This is required because conjugates are expected to occur with both soluble and insoluble plant constituents. Such a hydrolysis step must be incorporated into all methods to be used for data collection in support of tolerances. The method(s) selected for 3-chloroaniline analysis must be validated by submission of data relating to specificity, sensitivity, precision, and accuracy; one approach may be to spike radiolabeled 3-chloroaniline prior to extraction and hydrolysis if one of the existing methods for chlorpropham analysis is used. The analytical methodology used for generating the requested residue data for potato commodities must be appropriately validated (by using weathered labeled residues) and should be suitable for enforcement purposes. The method(s) chosen as suitable for enforcement must be validated by an independent laboratory prior to undergoing Agency validation.
- o If the requested data regarding the nature of the residues in plants and animals reveal the occurrence of additional metabolites of concern, additional analytical methods for data collection and enforcement may be required.

The Chlorpropham Guidance Document also required multiresidue protocol testing of chlorpropham and its metabolite isopropyl-OH-CIPC. The Pesttrak data base (PAM, Vol. I, Appendix, dated November 6, 1990) indicates chlorpropham is completely recovered

(> 80%) using Multiresidue Protocols D and E, whereas no data have been submitted for isopropyl-OH-CIPC. The following data requirements remain outstanding:

- o Isopropyl-OH-CIPC must be subjected to FDA Multiresidue Protocols C, D, and E. Multiresidue protocols are available from National Technical Information Service under order No. PB 203734/AS.

References (used):

N/A.

Discussion of the data:

N/A.

STORAGE STABILITY DATA

Conclusions:

The Chlorpropham Guidance Document dated December, 1987 required that storage intervals and conditions be supplied for all required and previously submitted residue chemistry data. Subsequent to the Guidance Document, the Agency again specified the need for these data for potatoes, owing to inconsistent and variable results obtained from the prior stability studies cited in the Residue Chemistry Chapter dated August 14, 1987 (H. Fonouni, CBRS No. 6272, dated April 4, 1990). No storage stability data have been submitted in response to the requirements; however, the Chlorpropham Task Force indicated the intent to submit data by July 15, 1991 (W. Smith, CBRS No. 7432, dated March 13, 1991). The requirements specified in the Guidance Document are reiterated below:

- o All requested plant and animal residue data must be accompanied by data regarding storage interval and conditions of sample storage. Data must also be submitted depicting the stability of chlorpropham residues of concern (including 3-chloroaniline) under the conditions and for the time intervals specified. In laboratory tests using fortified samples, the pure active ingredient and pure metabolites must be used; however, if field-weathered samples are used, the test substance must be a typical end-use product. If the requested metabolism data indicate the presence of additional residues of toxicological concern in plant and animal commodities, data depicting the stability of such residues in storage will be required.

References (used):

N/A.

Discussion of the data:

N/A.

MAGNITUDE OF THE RESIDUE IN PLANTS

The Chlorpropham Guidance Document dated December, 1987 required magnitude of residue data for 18 of the plant commodities registered for chlorpropham application. In response to the Guidance Document, the registrants voluntarily canceled all uses of chlorpropham on alfalfa, beans (succulent and dried), blackberries, blueberries, carrots, clover, cranberries, garlic, grasses, onions, peas, raspberries, rice, safflower, soybeans, spinach, sugar beets, and tomatoes, and indicated the intent to only support postharvest applications to potatoes (H. Fonouni, CBRS No. 6272, dated April 4, 1990; SPO5 Site Listing dated March 14, 1991). The Guidance Document requirements for data depicting the residues in or on the raw and processed commodities of potatoes following postharvest applications of EC and RTU formulations to potatoes in commercial storage were confirmed in this review.

The USDA requested clarification of data required to support a single at-planting broadcast application of chlorpropham to carrots grown in all domestic regions and to spinach grown in all domestic regions except CA (P. Deschamp, CBRS No. 7803, dated April 9, 1991). The reviewer reevaluated the requirements and concluded that a full complement of residue data are needed to support the indicated uses on carrots and spinach.

No residue chemistry data have been submitted in response to the 1987 Guidance Document requirements; however, the Chlorpropham Task Force indicated the intent to submit data for potatoes by July 15, 1993 (W. Smith, CBRS No. 7432, dated March 13, 1991).

The residue chemistry data requirements for potatoes and spinach discussed in this update are based on the food/feed use sites listed on the labels for currently registered products. When end-use product DCIs are developed (e.g., at issuance of the RED), RD should require that all end-use product labels (e.g., any unamended basic producer labels, SLNs, and products covered under the generic data exemption) be amended such that they are consistent with the labels supported by the basic producer.

Note to SRRD: A permanent tolerance has been established for residues of chlorpropham and its metabolite 1-hydroxy-2-propyl-3-chlorocarbanilate (calculated as residues of chlorpropham) in or on soybeans (40 CFR §180.181). Because chlorpropham is no longer registered for use on soybeans, we recommend that this tolerance be revoked.

Note to SRRD: Interim tolerances are in effect for residues of chlorpropham in or on alfalfa, alfalfa hay, beans (dry and succulent), blackberries, blueberries, clover, clover hay, cranberries, garlic, grass, grass hay, onions, peas (dry and succulent), raspberries, rice grain, safflower seed, sugar beet tops, sugar beet roots, and tomatoes (40 CFR §180.319).

Because chlorpropham is no longer registered for use on the aforementioned crops, we recommend that these tolerances be revoked. Interim tolerances are also in effect for residues of chlorpropham in or on carrots and spinach. In view of the existing use on spinach permitted under EPA SLN No. VA910004 and UDSA's wish to support chlorpropham use on carrots and spinach, we recommend that the interim tolerances for carrots and spinach remain in effect until appropriate permanent tolerances are established.

MAGNITUDE OF THE RESIDUE IN MEAT, MILK, POULTRY, AND EGGS

Tolerances:

Interim tolerances of 0.05 ppm have been established for residues of chlorpropham in or on eggs, milk, and the meat, fat, and meat byproducts of cattle, goats, hogs, horses, poultry, and sheep (40 CFR §180.319).

Conclusions:

The Chlorpropham Guidance Document dated December, 1987 reserved requirements for data depicting magnitude of residues in meat, milk, poultry, and eggs, pending the results of the required animal metabolism studies. Subsequent to the Guidance Document, the Agency again reserved requirements for these data (H. Fonouni, CBRS No. 6272, dated April 4, 1990). No magnitude of residue data have been submitted in response to the requirements; however, the Chlorpropham Task Force indicated the intent to submit data by July 15, 1992 (W. Smith, CBRS No. 7432, dated March 13, 1991). The comment for this topic in the Guidance Document is reiterated below:

- o The nature of the residue in animals is not adequately understood. Upon receipt of the data requested in the section "Nature of the Residue in Animals" the need for and nature of permanent tolerances for chlorpropham residues of concern in livestock will be assessed.

References (used):

N/A.

Discussion of the data:

N/A.

MAGNITUDE OF THE RESIDUE IN DRINKING AND IRRIGATION WATER

Tolerances:

No tolerances have been established for residues of chlorpropham in drinking and irrigation water.

Conclusions:

The Chlorpropham Guidance Document dated December, 1987 required data depicting magnitude of residues in drinking and irrigation water. In response to the Guidance Document, the registrants voluntarily canceled the aquatic use of chlorpropham on cranberries that had prompted these requirements. In reevaluating Guidance Document requirements, taking into account this use cancellation, the Agency concluded that residue data are no longer required for drinking and irrigation water (H. Fonouni, CBRS No. 6272, dated April 4, 1990).

References (used):

N/A.

Discussion of the data:

N/A.

MAGNITUDE OF THE RESIDUE IN FISH AND SHELLFISH

Tolerances:

No tolerances have been established for residues of chlorpropham in fish and shellfish.

Conclusions:

The Chlorpropham Guidance Document dated December, 1987 required data depicting magnitude of residues in fish and shellfish. In response to the Guidance Document, the registrants voluntarily canceled the aquatic use of chlorpropham on cranberries that had prompted these requirements. In reevaluating Guidance Document requirements, taking into account this use cancellation, the Agency concluded that residue data are no longer required for fish and shellfish (H. Fonouni, CBRS No. 6272, dated April 4, 1990).

References (used):

N/A.

Discussion of the data:

N/A.

TOLERANCE REASSESSMENT SUMMARY

The Chlorpropham Guidance Document dated December, 1987, and a subsequent Agency reevaluation of residue chemistry requirements for chlorpropham (H. Fonouni, CBRS No. 6272, dated April 4, 1990), concluded that the nature of the residue is adequately understood for growing plants, but is not adequately understood for potato tubers treated postharvest. The nature of the residue in animals is not adequately understood.

Additional data are required to support the established tolerance for residues in or on potatoes.

A permanent tolerance has been established for residues of chlorpropham in or on soybeans. Because chlorpropham is no longer registered for use on soybeans, we recommend that this tolerance be revoked.

Interim tolerances are in effect for residues of chlorpropham in or on alfalfa, alfalfa hay, beans (dry and succulent), blackberries, blueberries, clover, clover hay, cranberries, garlic, grass, grass hay, onions, peas (dry and succulent), raspberries, rice grain, safflower seed, sugar beet tops, sugar beet roots, and tomatoes (40 CFR §180.319). Because chlorpropham is no longer registered for use on the aforementioned crops, we recommend that these tolerances be revoked.

Permanent tolerances will be proposed for residues in or on carrots, and spinach based on residue data to support those uses.

Interim tolerances are also in effect for residues of chlorpropham in or on the eggs, milk, and meat, fat, and meat byproducts of cattle, goats, hogs, horses, poultry, and sheep (40 CFR §180.319). Upon receipt of the data requested in the section "Nature of the Residue in Animals" the need for and nature of permanent tolerances for chlorpropham residues of concern in livestock will be assessed.

No food/feed additive tolerances have been established for residues of chlorpropham. We cannot at this time make a recommendation regarding the need for such tolerances because requirements for data depicting the nature and magnitude of chlorpropham residues of concern in processed potato commodities remain outstanding.

MASTER RECORD IDENTIFICATION NUMBERS

A search of the Pesticide Document Management System (PDMS) conducted on July 16, 1991 revealed that no MRID documents pertaining to residue chemistry were submitted in response to the Chlorpropham Guidance Document dated December, 1987.

Residue Chemistry Citations (used):

N/A.

Residue Chemistry Citations (not used):

N/A.

AGENCY MEMORANDA

CBRS No. 6272
Subject: Chlorpropham Registration Standard: Response to the Product and Residue Chemistry Data Requirements
From: H. Fonouni
To: J. Coombs and R. Engler
Dated: April 4, 1990
MRID(s): N/A

CBRS No. 7432
Subject: Chlorpropham Registration Standard: Time Extension Request for Residue Chemistry Requirements
From: W. Smith
To: K. Farmer
Dated: March 13, 1991
MRID(s): N/A

CBRS No. 7803
Subject: Chlorpropham Registration Standard. USDA Request for Clarification of Product and Residue Chemistry Data Requirements
From: P. Deschamp
To: K. Farmer
Dated: April 9, 1991
MRID(s): N/A

TABLE A. GENERIC DATA REQUIREMENTS FOR CHLORPROPHAM RESIDUE CHEMISTRY.¹

Data Requirement	Test Substance ²	Does EPA have data to satisfy this requirement?	Bibliographic Citation ³	Must additional data be submitted under FIFRA Sec. 3(c)(2)(B)?
<u>40 CFR §158.240 Residue Chemistry</u>				
171-2. Chemical Identity ⁴				
171-3. Directions for Use	EP	Partially	N/A	Yes ⁵
171-4. Nature of the Residue (Metabolism)	Plants	Partially	N/A	Yes ⁴
	Livestock	Partially	N/A	Yes ⁷
171-4. Residue Analytical Methods				
Plant Residues	PGAI & Metabolites	Partially	N/A	Yes ^{9,10}
Animal Residues	PGAI & Metabolites	Partially	N/A	Reserved ^{9,10}
171-4. Storage Stability	TEP & Metabolites	Partially	N/A	Yes ¹¹
171-4. Magnitude of the Residue in Plants				
Root and Tuber Vegetables				
- Carrots	TEP	No	N/A	No ¹²
- Potatoes (processed commodities)	TEP	Partially	N/A	Yes ¹³
- Sugar beet roots (processed commodities)	TEP	No	N/A	Yes ¹⁴
	TEP	No	N/A	No ¹⁵
	TEP	No	N/A	No ¹⁵

(Continued, Footnotes Follow)

TABLE A. (Continued)

Data Requirement	Test Substance ²	Does EPA have data to satisfy this requirement?	Bibliographic Citation ³	Must additional data be submitted under FIFRA Sec. 3(c)(2)(B)?
Leaves of Root and Tuber Vegetables				
- Sugar beet tops	TEP	No	N/A	No ¹⁵
Bulb Vegetables				
- Garlic	TEP	No	N/A	No ¹⁵
- Onions	TEP	No	N/A	No ¹⁵
Leafy Vegetables				
- Spinach	TEP	No	N/A	Yes ¹⁶
Legume Vegetables				
- Beans (succulent and dried)	TEP	No	N/A	No ¹⁵
- Peas	TEP	No	N/A	No ¹⁵
- Soybeans (processed commodities)	TEP	No	N/A	No ¹⁷
Fruiting Vegetables				
- Tomatoes (processed commodities)	TEP	No	N/A	No ¹⁵
- Small Fruits and Berries	TEP	No	N/A	No ¹⁵
- Blackberries	TEP	No	N/A	No ¹⁵
- Blueberries	TEP	No	N/A	No ¹⁵
- Cranberries	TEP	No	N/A	No ¹⁵
- Raspberries	TEP	No	N/A	No ¹⁵

(Continued, Footnotes Follow)

TABLE A. (Continued)

Data Requirement	Test Substance ²	Does EPA have data to satisfy this requirement?	Bibliographic Citation ³	Must additional data be submitted under FIFRA Sec. 3(c)(2)(B)?
Cereal Grains				
- Rice (processed commodities)	TEP	No	N/A	No ¹⁵
Grass Forage, Fodder, and Hay	TEP	No	N/A	No ¹⁵
- Grass forage and hay	TEP	No	N/A	No ¹⁵
Nongrass Animal Feeds				
- Alfalfa forage and hay	TEP	No	N/A	No ¹⁵
- Birdsfoot trefoil forage and hay	TEP	No	N/A	No ¹⁸
- Clover forage and hay	TEP	No	N/A	No ¹⁵
Miscellaneous Commodities				
- Safflower seed	TEP	No	N/A	No ¹⁵
(processed commodities)	TEP	No	N/A	No ¹⁵
- Tobacco	TEP	Yes	N/A	No ¹⁹
171-4. Magnitude of the Residue in Meat/Milk/Poultry/Eggs	PAH & Plant Metabolites	Partially	N/A	Reserved ²⁰
171-4. Magnitude of the Residue in Drinking and Irrigation Water	TEP	No	N/A	No ²¹
171-4. Nature and Magnitude of the Residue in Fish and Shellfish	TEP	No	N/A	No ²¹

(Continued, Footnotes Follow)

TABLE A. (Continued)

¹No residue chemistry data have been submitted in response to the Chlorpropham Guidance Document dated December, 1987. Currently, the only food/feed use sites are stored potatoes and dormant spinach grown in VA. The registrants have indicated the intent to comply with all appropriate data requirements. Those data gaps for which no data have been submitted and that are carried over in this Update are indicated in shaded print.

²Test substance: TGAI = technical grade of the active ingredient; PAI = pure active ingredient; PAIRA = pure active ingredient, radiolabeled; TEP = typical end-use product; EP = end-use product.

³No data pertaining to residue chemistry were submitted in response to the Chlorpropham Guidance Document dated December, 1987.

⁴The same chemical identity data are required under 40 CFR 158.150-190, with emphasis on impurities that could constitute residue problems. Refer to product chemistry data requirements tables.

⁵The residue chemistry data requirements for potatoes and spinach discussed in this update are based on the food/feed use sites specified on the labels of currently registered products. When end-use product DCIs are developed (e.g., at issuance of the RED), RD should require that all end-use product labels (e.g., any unamended basic producer labels, SLNs, and products covered under the generic data exemption) be amended such that they are consistent with the labels supported by the basic producer.

⁶The registrants have indicated the intent to submit plant metabolism data by August 15, 1991 (W. Smith, CBRS No. 7432, dated March 13, 1991). Data must be submitted depicting the uptake, distribution, and metabolism of ring-labeled [¹⁴C]chlorpropham in stored potatoes following postharvest application at a rate sufficiently high to permit complete ¹⁴C-residue characterization. Representative samples from the required metabolism studies must also be analyzed using accepted enforcement methods to ascertain that these methods will determine all possible metabolites of concern, including any bound/conjugated residues of concern.

⁷The registrants have indicated the intent to submit animal metabolism data by December 15, 1991 (W. Smith, CBRS No. 7432, dated March 13, 1991). Metabolism studies must be submitted utilizing ruminants and poultry. Animals must be dosed for a minimum of 3 days with ring-labeled [¹⁴C]chlorpropham at a level sufficient to make identification and quantification of residues possible. Milk and eggs must be collected for analysis twice daily during the dosing period, and animals must be sacrificed within 24 hours after administration of the final dose. The distribution and identity of residues must be determined in milk,

TABLE A. (Continued)

liver, kidney, muscle, and fat of ruminants, and in eggs, liver, kidney, muscle, and fat of poultry. Samples from the requested animal metabolism studies must also be analyzed using current enforcement methods to determine the usefulness of these methods for analysis of animal commodities. The enforcement method must be capable of determining all free and bound/conjugated residues of concern.

⁸The registrants have indicated the intent to submit plant residue analytical methods by July 15, 1991, and animal residue analytical methods by January 15, 1992 (W. Smith, CBRS No. 7432, dated March 13, 1991). The registrant must select the specific method(s) recommended for tolerance enforcement. The method must include a hydrolysis step at the tissue stage to release bound/conjugated residues. Spiking may not produce conjugates. Therefore, enforcement methods must be tested in conjunction with plant and animal metabolism studies. The efficiency of extraction of bound/conjugated residues of concern must be determined for any or all residue data collection methods the registrant has used or will use to support tolerances. Residues must be "weathered" and not simply spiked into samples prior to analysis. This may best be conducted in conjunction with plant and animal metabolism studies involving radiolabeled material. This is required because conjugates are expected to occur with both soluble and insoluble plant constituents. Such a hydrolysis step must be incorporated into all methods to be used for data collection in support of tolerances. The method(s) selected for 3-chloroaniline analysis must be validated by submission of data relating to specificity, sensitivity, precision, and accuracy; one approach may be to spike radiolabeled 3-chloroaniline prior to extraction and hydrolysis if one of the existing methods for chloroprotham analysis is used. The analytical methodology used for generating the requested residue data for potato commodities must be appropriately validated (by using weathered labeled residues) and should be suitable for enforcement purposes. The method(s) chosen as suitable for enforcement must be validated by an independent laboratory prior to undergoing Agency validation.

⁹If the requested data regarding the nature of the residues in plants and animals reveal the occurrence of additional metabolites of concern, additional analytical methods for data collection and enforcement may be required.

¹⁰Isopropyl-OH-CIPC must be subjected to FDA Multiresidue Protocols C, D, and E. Multiresidue protocols are available from National Technical Information Service under order No. PB 203734/AS.

¹¹The registrants have indicated the intent to submit storage stability data by July 15, 1991 (W. Smith, CBRS No. 7432, dated March 13, 1991). All requested plant and animal residue data must be accompanied by data regarding storage interval and conditions of sample storage. Data must also be submitted depicting the stability of chloroprotham residues of concern (including 3-chloroaniline) under the conditions and for the time intervals specified. In laboratory tests using fortified samples, the pure active ingredient and pure metabolites must be used; however, if field-weathered samples are used, the test substance must be a

TABLE A. (Continued)

typical end-use product. If the requested metabolism data indicate the presence of additional residues of toxicological concern in plant and animal commodities, data depicting the stability of such residues in storage will be required.

- ¹²Chlorpropham is no longer registered for use on carrots. In view of USDA's wish to support chlorpropham use on carrots, we recommend that the interim tolerance for carrots remain in effect.
- ¹³The registrants have indicated the intent to submit residue data for potatoes by July 15, 1993 (W. Smith, CBRS No. 7432, dated March 13, 1991). Data are required depicting chlorpropham residues of concern (including 3-chloroaniline) in or on potatoes analyzed immediately after treatment in commercial storage with an RTU formulation applied at the maximum registered rate as an aerosol through forced air circulation systems, and (in separate tests) an EC formulation applied at the maximum registered rate as a dilute aqueous spray to potatoes moved along a conveyor belt. Samples from each test must be taken from several positions in the storage pile.
- ¹⁴The registrants have indicated the intent to submit data for potatoes by July 15, 1993. A processing study is required depicting chlorpropham residues of concern (including 3-chloroaniline) in potato granules, potato chips, and potato peels (wet and dried) processed from raw tubers bearing measurable, weathered residues. If residues concentrate in any of these processed commodities, the registrant must propose an appropriate food/feed additive tolerance.
- ¹⁵NOTE TO SRRD: Chlorpropham is no longer registered for use on the following commodities: alfalfa, alfalfa hay, beans (succulent and dried), blackberries, blueberries, clover hay, clover, cranberries, garlic, grass hay, grasses, onions, peas, raspberries, rice, safflower, sugar beet tops, sugar beet roots, and tomatoes; therefore, the interim tolerances in 40 CFR §180.319 should be revoked.
- ¹⁶No data have been submitted in response to the Guidance Document. The following additional data remain outstanding to support the use of chlorpropham on spinach in VA under EPA SLN No. VA910004: Data depicting chlorpropham residues of concern in or on spinach harvested 30 days after application of the 4 lb/gal EC formulation at the maximum registered use rate using conventional ground equipment. Tests must be conducted in VA. The registrant must propose an appropriate permanent tolerance for chlorpropham residues of concern in or on spinach.
- ¹⁷NOTE TO SRRD: Chlorpropham is no longer registered for use on soybeans; therefore, the permanent tolerance in 40 CFR §180.181 should be revoked.

TABLE A. (Continued)

¹⁸Chlorpropham is no longer registered for use on birdsfoot trefoil, nor have any tolerances been established for chlorpropham residues in or on birdsfoot trefoil. No data are required.

¹⁹Chlorpropham is no longer registered for use on tobacco. No data are required.

²⁰The registrants have indicated the intent to submit residue data for animals by July 15, 1992. However, the nature of the residue in animals is not adequately understood. Upon receipt of the data requested in the section "Nature of the Residue in Animals" the need for and nature of permanent tolerances for chlorpropham residues of concern in livestock will be assessed.

²¹Chlorpropham is no longer registered for the aquatic use on cranberries that had prompted the Chlorpropham Guidance Document dated December, 1987 requirement for irrigation water, potable water, fish, and shellfish. No data are required.