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

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

MEMORANDUM

Date: January 9, 2007

Subject: Lactofen. Addition of New Uses: Fruiting Vegetables (Crop Group 8) and Okra. PRIA R17. Summary of Analytical Chemistry and Residue Data. PP#5E6930.

DP Barcode:	D333151	Decision Number:	356302
PC Code:	128888	MRID Nos.:	46531301 and 46597201-46597203
40 CFR 180.	432		
Chemical Class:	Diphenyl ether herbicide (Group 14)		

From: Christine L. Olinger, Chemist
Reregistration Branch 1
Health Effects Division (7509P)

Through: Donna Davis, Chemist
Reregistration Branch 1
Health Effects Division (7509P)

Michael S. Metzger, Chief
Reregistration Branch 1
Health Effects Division (7509P)

To: Dan Kenny/Joanne Miller
Herbicide Branch
Registration Division (7505P)

This document was originally prepared under contract by Dynamac Corporation (2275 Research Blvd, Suite 300; Rockville, MD 20850; submitted 07/18/2006). The document has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

Executive Summary

Lactofen is a selective contact, diphenyl ether herbicide (Group 14) that is structurally related to acifluorfen and is classified as a threshold carcinogen by EPA (Lactofen - Report of the Cancer Assessment Review Committee; 5/22/02). Lactofen is currently registered by Valent U.S.A. Corporation for preemergence and/or postemergence use on cotton, peanuts, snap beans, and soybeans for the control of broadleaf weeds, such as nightshades, morning glories, pigweed, and ragweed.

Valent U.S.A. corporation, in coordination with the Interregional Research Project No. 4 (IR-4), has proposed to amend the use pattern for the 2 lb/gal emulsifiable concentrate (EC) formulation of lactofen (Cobra® Herbicide; EPA Reg. No. 59639-34) to include uses on fruiting vegetables (Crop Group 8) and okra in AL, AR, FL, GA, MS, NC, SC, TN, and VA. The proposed uses include directed, shielded application to row middles made pre- or post-transplant at 0.3-0.5 lb ai/A/application for a maximum seasonal application rate of 1.0 lb ai/A. A 30-day PHI is proposed.

In conjunction with the amended use request, IR-4 has proposed, in PP#5E6390, the establishment of permanent tolerances for the residues of lactofen and its associated metabolites containing the diphenyl ether linkage expressed as lactofen in/on the following raw agricultural commodities:

Vegetable, fruiting, group	0.01 ppm
Okra	0.01 ppm

Tolerances for residues of lactofen in/on raw agricultural commodities are established under 40 CFR §180.432(a) and are expressed in terms of the herbicide lactofen, 1-(carboethoxy)ethyl 5-[2-chloro-4-(trifluoromethyl)phenoxy]-2-nitrobenzoate. Tolerances are established for snap bean, cotton seed, peanut, and soybean seed at 0.01 ppm, and for cotton gin products at 0.02 ppm [40 CFR §180.432(a)].

The qualitative nature of the residue of lactofen in plants is adequately understood based on acceptable studies depicting the metabolism of [^{14}C]lactofen in soybeans, peanuts, and tomatoes. Although the quantities of individual metabolites vary between crops, the data indicate that the metabolic pathway is similar between crops. The metabolism of lactofen initially involves reduction of the nitro group to an amino group, with or without loss of the ethyl ester side chains to form the preliminary diphenyl ether metabolites: amino lactofen (PPG-1576), N-formyl lactofen (PPG-2597), desethyl lactofen (PPG-947), acifluorfen (PPG-947), and amino acifluorfen (PPG-2053). Subsequent conjugation of these primary metabolites through their carboxyl and amino groups results in the formation of complex soluble and insoluble polar components. Following formation of acifluorfen, the diphenyl ether bond may be cleaved in a glutathione-mediated reaction to form a glutathione conjugate with the 2-nitrobenzoic acid moiety. Subsequent degradation of the glutathione moiety to cysteine forms S-(carboxy-4-nitrophenyl)cysteine (CNPC).

The tolerance expression for lactofen formerly included lactofen and metabolites containing the diphenyl ether linkage. In 2000, HED concluded that only the parent compound need be included in the tolerance expression and risk assessment for plant commodities, assuming the

pre-harvest interval is 45 days or greater.

Although the proposed use of lactofen on fruiting vegetables reflects a 30-day PHI, based on the available crop field trial data reflecting nonquantifiable residues in tomato and pepper, HED concludes that the tolerance expression for fruiting vegetables and okra need only include parent lactofen.

There are no livestock feedstuffs associated with the proposed uses on fruiting vegetables and okra. Therefore, no livestock metabolism data, enforcement methods, storage stability data, or feeding studies are required to support this petition.

Acceptable gas chromatography with electron capture detection (GC/ECD) methods are available in the Pesticide Analytical Manual (PAM) Vol. II for the enforcement of tolerances of lactofen and metabolites in plant commodities. A modified version of Method B is listed in the U.S. EPA Index of Pesticide Analytical Methods under lactofen. Samples from the pepper and tomato field trials were analyzed using established GC/ECD enforcement methods or modified versions of established enforcement methods. The validated limits of quantitation (LOQs) were 0.01 ppm for peppers from the 1991 trial, and 0.02 ppm for samples from all other trials. The methods are adequate for data collection based on acceptable method validation and concurrent recovery data.

The maximum storage intervals of samples of peppers and tomatoes from harvest to analysis were 60 days for peppers and 56 days for tomatoes. A concurrent freezer storage stability study was conducted in conjunction with the 1990 magnitude of the residue study on tomatoes, which demonstrated that residues of lactofen and metabolites PPG-847, PPG-947, and PPG-2597 were relatively stable in/on tomatoes stored frozen for up to 68 days; residues of PPG-1576 were found to decline (~40%) during storage for 68 days. The submitted data are adequate to support the storage intervals and conditions of samples from the fruiting vegetable crop field trials.

The submitted crop field trial data for pepper and tomato do not meet the recommendations in the guidance for guideline no. 860.1500 because of inadequate geographic representation. However, due to the very low residues, and the available data are in a region to that similar to those requested in this petition for a tolerance with a regional registration, HED will not request any additional data for the proposed use. Although inadequate, the data indicate that residues of lactofen were below the LOQ (<0.01-<0.02 ppm) in/on samples following application of lactofen according to the proposed use pattern.

No crop field trial data were submitted to support the proposed use on okra. Okra will be added to the fruiting vegetable crop group (Personal communication, B. Schneider 10/13/06), so the tomato and pepper data may be translated to okra.

Additional data/information are required to support the available confined rotational and limited rotational crop data; however, the available data indicate that the nature of the residue in rotational crops is adequately understood and that plantback intervals are not needed for the proposed use on fruiting vegetables.

Regulatory Recommendations and Residue Chemistry Deficiencies

HED has examined the residue chemistry database for lactofen. Pending submission of a revised Section B (see requirements under Directions for Use) and a revised Section F (see requirements under Proposed Tolerances), **there are no residue chemistry issues that would preclude granting unconditional regional registration for the requested use of lactofen on the fruiting vegetables crop group and okra in AL, AR, FL, GA, MS, NC, SC, TN, and VA or establishment of tolerances with regional registration for residues of lactofen per se as follows:**

Vegetable, fruiting, group 8 .....0.02 ppm
Okra .....0.02 ppm

Note that the tolerances for regional registration should be placed in section (c) of 180.432.

A human health risk assessment is forthcoming.

860.1200 Directions for Use

- The label must be amended to specify that the applications may not include two post-transplant applications. Finally, the label must be amended to reflect either a 30-day RTI or a minimum post-transplant interval of 18 days for tomatoes.
- The label should specify examples of fruiting vegetables in the use directions to avoid confusion.

OPPTS 860.1550 Proposed Tolerances

- **The proposed tolerance for the fruiting vegetables crop group should be revised to reflect the recommended tolerance expression and the correct commodity definition, "Vegetable, fruiting, group 8," and the recommended level of 0.02 ppm.**
- **The proposed tolerance for okra should be revised to reflect the recommended tolerance expression and the recommended level of 0.02 ppm.**

860.1500 Crop Field Trials

- If the petitioner wishes to pursue a national section 3 registration then at least one trial with a small-fruited tomato should be submitted with the additional field trials.

Background

The chemical structure and nomenclature of lactofen are presented in Table 1. The physicochemical properties of the technical grade of lactofen are presented in Table 2.

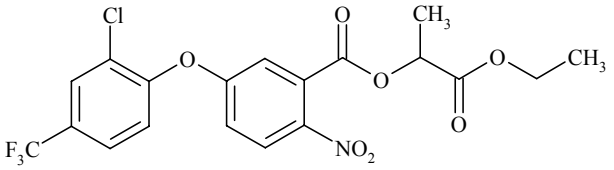
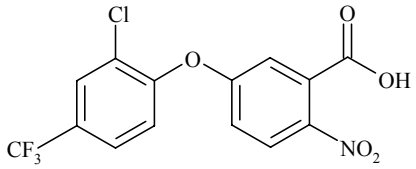
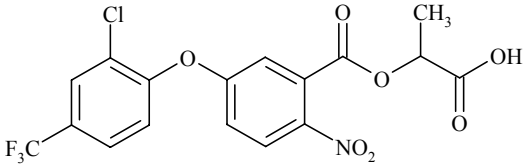
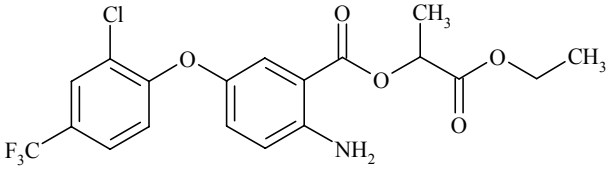
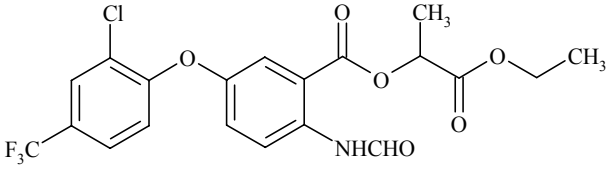
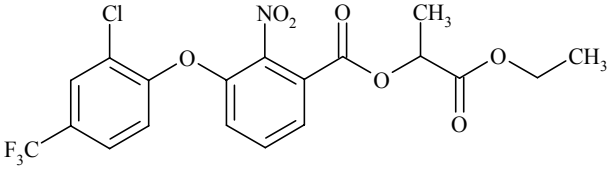
Table 1. Lactofen Nomenclature.	
Chemical structure	
Common name	Lactofen
Company experimental name	PPG-844
IUPAC name	ethyl O-[5-(2-chloro-α,α,α-trifluoro-p-tolyloxy)-2-nitrobenzoyl]-DL-lactate
CAS name	2-ethoxy-1-methyl-2-oxoethyl 5-[2-chloro-4-(trifluoromethyl)phenoxy]-2-nitrobenzoate
CAS registry number	77501-63-4
End-use product (EP)	2 lb/gal EC (Cobra ® Herbicide; EPA Reg. No. 59639-34)
Chemical structure of acifluorfen (PPG-847)	 5-[2-chloro-4-(trifluoromethyl)phenoxy]-2-nitrobenzoic acid
Chemical structure of desethyl lactofen (PPG-947)	 1-(carboxy)ethyl 5-[2-chloro-4-(trifluoromethyl)phenoxy]-2-nitrobenzoate
Chemical structure of amino lactofen (PPG-1576)	 1-(carboethoxy)ethyl 5-[2-chloro-4-(trifluoromethyl)phenoxy]-2-aminobenzoate
Chemical structure of N-formyl lactofen (PPG-2597)	 1-(carboethoxy)ethyl 5-[2-chloro-4-(trifluoromethyl)phenoxy]-2-formamidobenzoate
Chemical structure of PPG-1530; Isomer A (internal standard)	 1-(carboethoxy)ethyl 5-[2-chloro-4-(trifluoromethyl)phenoxy]-6-nitrobenzoate

Table 2. Physicochemical Properties of Lactofen.		
Parameter	Value	Reference
Melting point/range	>250°C	44447003[1]
pH	7.2 (on Pure Active Ingredient, 1% solution) at 25°C	44447003[1]
Density (specific gravity)	1.34 at 24°C	44447003[1]
Water solubility	0.97 ppm at 25°C 0.945 ± 0.131 ppm (column elution method at 20 ± 1 °C)	44447003[1] 44460902[2]
Solvent solubility	g/100 g at 23 °C kerosene 15.6 2-ethyl-1-hexanol 18.4 N-decanol 10.1 lactic acid 0.9 Lactofen is miscible at all proportions with the following solvents at -18°C or higher: DMSO, monochlorotoluene, dipropylene glycol dibenzoate, isophorone, cyclohexanone, mixed xylene, ethylene dichloride, acetone, DMF, amyl acetate, methyl isobutyl ketone.	44447003[1]
Vapor pressure	3.69 ± 1.73 x 10^{-5} Pa (2.8 x 10-7 mm Hg)	44460901[2]
Dissociation constant, pK_a	Not required	D241826, 1/16/98, H. Podall
Octanol/water partition coefficient, Log(K_{OW})	1 x 10^5 at ambient temperature, estimated value	44460903[2]
UV/visible absorption spectrum	In Review [3]	44447003[3]

[1] RD Memorandum, D241826, 1/16/98, H. Podall.
[2] RD Memorandum D242241, 2/5/98, S. Mathur.
[3] D332587, C. Olinger, In Review.

860.1200 Directions for Use

Valent has included the proposed used directions under Section B of the petition and a supplemental label for the 2 lb/gal EC formulation of lactofen (Cobra® Herbicide; EPA Reg. No. 59639-34). The proposed uses are presented in Table 3.

Table 3. Summary of Directions for Use of Lactofen.						
Applic. Timing; Type; and Equip.	Formulation [EPA Reg. No.]	Applic. Rate (lb ai/A)	Max. No. Applic. per Season	Max. Seasonal Applic. Rate (lb ai/A)	PHI (days)	Use Directions and Limitations
Fruiting vegetables and okra						
Pre-transplant Post-transplant; Directed to row middles; Ground, shielded	2 lb/gal EC [59639-34]	0.3-0.5	2	1.0 (implied)	30	Use is restricted to AL, AR, FL, GA, MS, NC, SC, TN, and VA. Applications are to be made in 20-50 gal/A. Pre-transplant: Applications are to be made a minimum of 10 days prior to transplanting. Post-transplant: Applications are to be made to using an adjuvant such as crop oil concentrate at 1% v:v or a nonionic surfactant at 0.25% v:v. Tomato plants must be at least 16" in height prior to post-transplant application. Peppers must have been transplanted at least 45 days before making a post-transplant application.

There are currently no plantback restrictions on the supplemental or master label (acceptance date 10/8/04)

Conclusions. The submitted information concerning the proposed use pattern is adequate to allow evaluation of the submitted data for fruiting vegetables and okra.

The label must be amended to specify that the applications may not include two post-transplant applications; the submitted crop field trial for peppers reflected only one post-transplant application. The available tomato field trial data reflect a 30- to 37-day RTI with post-transplant applications made 18-42 days after transplanting. The label must be amended to reflect either a 30-day RTI or a minimum post-transplant interval of 18 days for tomato. Finally, the label should provide examples of fruiting vegetables in the use directions (fruiting vegetables such as tomatoes, peppers, and eggplant).

860.1300 Nature of the Residue - Plants

D263857, 5/4/00, C. Olinger
D265469, 4/26/00, C. Olinger

Adequate studies are available depicting the metabolism of [^{14}C]lactofen in soybeans, peanuts, and tomatoes. Although the quantities of individual metabolites vary between crops, the data indicate that the metabolic pathway is similar between crops. The metabolism of lactofen initially involves reduction of the nitro group to an amino group, with or without loss of the ethyl ester side chains to form the preliminary diphenyl ether metabolites: amino lactofen (PPG-1576), N-formyl lactofen (PPG-2597), desethyl lactofen (PPG-947), acifluorfen (PPG-947), and amino acifluorfen (PPG-2053). Subsequent conjugation of these primary metabolites through their carboxyl and amino groups results in the formation of complex soluble and insoluble polar components. Additional data from a peanut metabolism study indicate that following formation of acifluorfen, the diphenyl ether bond may be cleaved in a glutathione-mediated reaction to form a glutathione conjugate with the 2-nitrobenzoic acid moiety. Subsequent degradation of the glutathione moiety to cysteine forms S-(carboxy-4-nitrophenyl)cysteine (CNPC), which was the most abundant metabolite detected in peanut hay. Free and conjugated 5-hydroxy-2-nitrobenzoic acid (HNBA) detected in nutmeats and hay may result from either loss of the cysteine moiety or from direct cleavage of the acifluorfen metabolite.

The tolerance expression for lactofen formerly included lactofen and metabolites containing the diphenyl ether linkage. Specifically, the enforcement method is capable of determining lactofen, acifluorfen (PPG-847), des-ethyl lactofen (PPG-947), amino lactofen (PPG-1576), and N-formyl lactofen (PPG-2597). In 2000 HED concluded that only the parent compound need be included in the tolerance expression and risk assessment for plant commodities, assuming the pre-harvest interval is 45 days or greater.

Conclusions. **Although the proposed use of lactofen on fruiting vegetables reflects a 30-day PHI, based on the available crop field trial data reflecting nonquantifiable residues in tomato and pepper, HED believes that the decision to include parent only in the tolerance expression for fruiting vegetables is appropriate**.

860.1300 Nature of the Residue - Livestock

There are no livestock feedstuffs associated with the proposed uses on fruiting vegetables and okra. Therefore, data requirements for livestock metabolism are not relevant to this tolerance petition.

860.1340 Residue Analytical Methods

D263857, 5/4/00, C. Olinger

Enforcement methods: The Pesticide Analytical Manual (PAM), Vol. II lists three GC/ECD methods (Methods I, A, and B) for determining residues of lactofen and metabolites in plant commodities. For Method I, residues of lactofen are extracted with acetonitrile:triethylamine (ACN:TEA, 99:1, v:v), followed by partitioning with hexane for oily matrices. Residues are then purified by silica gel column chromatography and analyzed by GC/ECD using a DB-5 column. The Agency validated this method down to a limit of 0.01 ppm using soybeans.

Method A is similar to Method I, except that the extracted residues are base (NaOH) hydrolyzed, converting lactofen to acifluorfen, which is then methylated with diazomethane. The derivatized residues are then purified by silica gel column chromatography and analyzed by GC/ECD using a DB-1701 column. Method B (Chevron Method RM-28, 3/12/90) is essentially identical to Method I, except that it allows for the use of an alternative column (DB-1701) with GC/ECD analysis for confirmation of residues.

In conjunction with the petitions for use of lactofen on cotton and peanuts, Method RM-28 was revised by changing the extraction solvent from ACN:TEA to ethanol:water:TEA (94:5:1, v:v:v) and adding a water:dichloromethane (DCM) partitioning step after solvent extraction. The modified method (RM-28B) was rewritten to clarify the procedures and renamed Method RM-28D. This method has been successfully radiovalidated and has undergone a successful independent laboratory validation and petition method validation (PMV). Method RM-28D is currently listed in the U.S. EPA Index of Pesticide Analytical Methods under lactofen.

Data collection methods: Samples from the pepper and tomato field trials were analyzed using established GC/ECD enforcement methods or modified versions of established enforcement methods. Pepper samples from the 1991 trial and tomato samples from the 1990 trials were analyzed for residues of lactofen and its metabolites PPG-1576, PPG-2597, PPG-847, and PPG-947 using method RM-28. The method was performed essentially as written for analysis of tomatoes, but was modified significantly for analysis of peppers. Modifications to the analytical method for peppers included: (1) conducting the ACN:hexane partitioning earlier in the procedure; (2) separation of the acid metabolites (PPG-847 and PPG-947) from lactofen and the ester metabolites (PPG-1576 and PPG-2597) for analysis; and (3) addition of a two-column clean-up procedure for the acid metabolites. Samples of peppers and tomatoes from the 2003 trials were analyzed for residues of lactofen *per se* using a modified version of method RM-28D: method RM-28D-2 (rev. 8/12/03).

Using the modified version of method RM-28, samples from the 1991 pepper field trial were extracted 2x with ACN containing 1% TEA:hexane (2:1, v:v) and filtered, and the extracts were combined. Following phase separation, the ACN phase was extracted with two additional aliquots of hexane; all hexane phases were discarded. The ACN extract was combined with 5% NaCl solution and partitioned 3x with hexane. The resulting extracts were combined to yield an aqueous ACN extract and a hexane extract. The hexane extracts, containing lactofen and the ester metabolites, were concentrated and applied to a silica gel column for clean-up. Residues were eluted with DCM:hexane (70:30, v:v), and the eluate was concentrated, combined with an internal standard mixture of CGA-1530 (lactofen Isomer A) and CGA-1827 (standard was not

identified), and reserved for GC analysis. The aqueous ACN extract, containing the acid metabolites, was acidified with 6 N HCl and extracted 3x with toluene. The combined toluene extracts were applied to a basic alumina column, and residues were eluted with 1% sodium bicarbonate solution. The eluate was acidified with 6 N HCl and extracted 3x with DCM. Diazomethane was added to the combined DCM extracts to methylate the acid metabolites, and the mixture was reduced to dryness and re-dissolved in benzene, then applied to a second alumina column. Residues were eluted with benzene, concentrated, combined with the internal standard mixture, and reserved for GC analysis. Lactofen and the ester metabolites were determined using an SPB-5 column, and the acid metabolites were determined using a DB-1701 column. The validated LOQ was 0.01 ppm (lowest limit of method validation; LLMV), and the reported LOD was 0.005 ppm for lactofen and each metabolite.

Using method RM-28, samples from the 1990 tomato field trials were extracted 2x with ACN containing 1% TEA and filtered. The resulting extract was evaporated to dryness, re-dissolved in 5% NaCl solution, then partitioned with DCM (3x). The resulting DCM phases were combined, reduced to dryness, dissolved in ACN, and combined with diazomethane to methylate the acid metabolites. The methylated extract was dissolved in DCM:hexane (70:30, v:v), and applied to a silica gel column. Residues were eluted with DCM:hexane (70:30, v:v), and the eluate was concentrated, combined with an internal standard of CGA-1530 in toluene, and reserved for GC analysis using a DB-5 or DB-1701 column. The validated LOQ (LLMV) was 0.02 ppm, and the LOD was 0.01 ppm for lactofen and each metabolite.

Using method RM-28D-2, samples of peppers and tomatoes from the 2003 trials were extracted 2x with ethanol and filtered. The combined extracts were reduced by rotary evaporation and sonicated with ACN saturated with hexane, followed by 5% NaCl solution, and hexane. The resulting ACN:water phase was re-extracted 2x with hexane, and the hexane extracts were combined with the original hexane phase. The combined hexane phase was evaporated to dryness and redissolved in toluene:hexane (1:2, v:v), then applied to a silica gel column for clean-up. Residues were eluted with hexane:diethyl ether (60:40, v:v), and the eluate was evaporated to dryness and dissolved in toluene for analysis by GC/ECD on a DB-17 column. The validated LOQ was 0.02 ppm (LLMV), and the reported LOD was 0.01 ppm for lactofen in both matrices.

Conclusions. The available and submitted residue analytical methods data are adequate to satisfy data requirements for purposes of the subject petition. Adequate tolerance enforcement methods are available for plant commodities, and residues of lactofen and metabolites were determined in the submitted crop field trial data using acceptable methods.

860.1360 Multiresidue Methods

Acceptable data are available on the recovery of lactofen and its four plant metabolites (PPG-847, PPG-947, PPG-1576, and PPG-2597) through Multiresidue Method Testing Protocols. The FDA PESTDATA database (dated 06/05) indicates that residues of lactofen *per se* are completely recovered through multiresidue method Section 304 (Protocol F); no data are available on the recovery of lactofen through Sections 302 and 303 (Protocols D and E. Metabolite PPG-1576 is partially recovered (54-85%) through Section 304 but metabolites PPG-847, PPG-947, and PPG-2597 are not recovered through Sections 303 and 304. Metabolite PPG-847 and PPG-947 are partially recovered (49-78%) through Section 402 (Protocol B).

860.1380 Storage Stability

A concurrent storage stability study was conducted with the crop field trials submitted in support of this action. Untreated samples of tomato from the 1990 magnitude of the residue study were fortified with lactofen, PPG-847, PPG-947, PPG-1576, and PPG-2597 at 0.1 ppm each, and stored frozen. Stored samples were analyzed at 0-day and following frozen storage for 32 and 68 days. Residues of lactofen, and all metabolites except PPG-1576 appeared to be relatively stable in/on tomatoes stored frozen for up to 68 days. Residues of PPG-1576 were found to decline in tomatoes, to ~60% of original value after 68 days of storage.

The maximum storage intervals of samples from harvest to analysis were 60 days for peppers and 56 days for tomatoes. Samples were stored frozen at ~-20 °C.

Conclusions. The submitted storage stability data are adequate to support the storage intervals and conditions of samples from the fruiting vegetable crop field trials. Because residues of PPG-1576 were found to be below the LOD in/on all tomato samples and below the LOQ in/on all pepper samples that were analyzed for residues of PPG-1576, no correction for potential decline during storage is needed.

860.1400 Water, Fish, and Irrigated Crops

There are no proposed/registered uses that are relevant to this guideline topic.

860.1460 Food Handling

There are no proposed/registered uses that are relevant to this guideline topic.

860.1480 Meat, Milk, Poultry, and Eggs

There are no livestock feedstuffs associated with the proposed use on fruiting vegetables and okra. Therefore, data requirements pertaining to meat, milk, poultry, and eggs are not relevant to this tolerance petition.

860.1500 Crop Field Trials

D265469, 4/26/00, C. Olinger
46531301.der.doc (includes review of MRIDs 46597201-46597203)

Table 4. Summary of Residue Data from Crop Field Trials with Lactofen

Crop matrix	Total Applic. Rate (lb ai/A)	PHI (days)	Residue Levels (ppm) of Lactofen per se						
			n	Min.	Max.	HAFT [1]	Median	Mean	Std. Dev.
Fruiting Vegetables Crop Group 8 (proposed use = 1.0 lb ai/A total application rate, 30-day PHI)									
Pepper	0.98-1.1	30	6	<0.01	<0.02	<0.02	<0.01	<0.01	0.0
Tomato	0.96	28-30	2	<0.02	<0.02	<0.02	<0.01	<0.01	0.0
	1.5	30	10	<0.02	<0.02	<0.02	<0.01	<0.01	0.0
	4.9	30	2	<0.02	<0.02	<0.02	<0.01	<0.01	0.0

[1] HAFT = Highest average field trial result.

Valent U.S.A. Corporation has submitted field trial data for lactofen on the representative crops, pepper and tomato, of the fruiting vegetables group, crop group 8. A total of three pepper trials were conducted in Zone 3 (FL) during the 1991 (one bell pepper trial) and 2003 (one bell and one nonbell pepper trial) growing seasons. A total of four tomato field trials were conducted in Zone 3 (FL) during the 1990 (three trials) and 2003 (one trial) growing seasons. Geographic representation is inadequate. All of the pepper and tomato field trials were conducted in Zone 3; however, the petitioner is proposing use of lactofen on fruiting vegetables in Zones 2, 3, and 4.

We note that both tomato varieties used in the crop field trials produce medium to large fruits.

For the pepper field trials, the 2 lb/gal EC formulation of lactofen was applied at each test location as one pre-transplant and one postemergence directed soil application to row middles at 0.49-0.51 lb ai/A/application for a total seasonal application rate of 0.98-1.1 lb ai/A (1x the maximum proposed seasonal application rate). Shielded spray equipment was used in the 2003 trials. The first applications were made one or 12 days prior to transplanting, and the second applications were made at 46- to 67-day retreatment intervals. First applications were made in spray volumes of 31-33 gal/A, and second applications were made in spray volumes of 55-59 gal/A; nonionic surfactant (NIS) or crop oil concentrate (COC) adjuvants were added to the spray mixtures for second applications. Mature peppers were harvested 30 days following the second application.

For the tomato field trials, the 2 lb/gal EC formulation of lactofen was applied at each test location as one pre- or early post-transplant application and one to two postemergence directed soil applications to row middles at ~0.5 lb ai/A/application for total seasonal application rates of 0.96 lb ai/A (2003 field trial) or 1.5 lb ai/A (1990 trials); the 2003 trial included a treatment plot with two applications at an exaggerated rate of ~2.5 lb ai/A/application for a total seasonal application rate of ~5 lb ai/A. The seasonal application rates of 1.0 and 1.5 lb ai/A correspond to 1x and 1.5x the maximum proposed seasonal application rate for fruiting vegetables. Shielded spray equipment was used for all trials. The first applications were made one or 12 days prior to transplanting or 5 days post-transplant; second applications were made at 30- to 37-day retreatment intervals; and third applications were made at 14- to 16-day retreatment intervals.

First applications were made in spray volumes of 31-34 gal/A, and second and third applications were made in spray volumes of 55-60 gal/A; NIS or crop COC adjuvants were added to the spray mixtures for all applications except the pre-transplant applications at the 2003 trial. Mature tomatoes were harvested 28-30 days following the last application.

The maximum storage intervals of samples from harvest to analysis were 60 days for peppers and 56 days for tomatoes. A freezer storage stability study was conducted in conjunction with the 1990 magnitude of the residue study on tomatoes. Residues of lactofen and metabolites PPG-847, PPG-947, and PPG-2597 appeared to be relatively stable in/on tomatoes stored frozen for up to 68 days. Residues of PPG-1576 were found to decline in tomatoes, to ~60% of original value after 68 days of storage. These data are adequate to support the storage intervals and conditions of samples from the fruiting vegetable crop field trials. Because residues of PPG-1576 were found to be below the LOD in/on all tomato samples and below the LOQ in/on all pepper samples that were analyzed for residues of PPG-1576, no correction for potential decline during storage is needed.

Samples from the pepper and tomato field trials were analyzed using established gas GC/ECD enforcement methods or modified versions of established enforcement methods. Pepper samples from the 1991 trial and tomato samples from the 1990 trials were analyzed for residues of lactofen and its metabolites PPG-1576, PPG-2597, PPG-847, and PPG-947 using method RM-28 (Method B of PAM Vol. II). The method was performed essentially as written for analysis of tomatoes, but was modified significantly for analysis of peppers. Samples of peppers and tomatoes from the 2003 trials were analyzed for residues of lactofen *per se* using method RM-28D-2 (rev. 8/12/03); method RM-28D is listed in the U.S. EPA Index of Pesticide Analytical Method. The validated LOQs were 0.01 ppm for peppers from the 1991 trial, and 0.02 ppm for samples from all other trials. The methods are adequate for data collection based on acceptable method validation and concurrent recovery data.

The results of the fruiting vegetable crop field trials are presented in Table 4. Residues of lactofen and metabolites were each below the LOQ (<0.01 ppm for the 1991 pepper field trials and <0.02 ppm for remaining pepper and tomato field trials) in/on all samples of pepper and tomato harvested ~30 days following a single pre- or early post-transplant and one to two postemergence directed soil applications to row middles at ~0.5 lb ai/A/application for total seasonal application rates of ~1-1.5 lb ai/A.

No residue decline data were included in the submission; however, because residues were below the LOQ in/on all samples, these data are not required.

Conclusions. Although the submitted pepper and tomato crop field trial data are inconsistent with the recommended data in the crop field trial guidance, due to the early season use and lack of detectable residues, they are sufficient for a tolerance with a regional registration requested by the petitioner.

For the proposed use on fruiting vegetables, soil characteristics data were not provided for two pepper field trials and one tomato trial; however, these data are not required at this time because most of the relevant information is available from a reliable public source. For future submissions, the petitioner is advised that soil characteristics data must be provided for field trials reflecting applications to soil. Although only one of the three tomato field trials reflected

application according to the proposed use pattern (two applications at a maximum seasonal rate of 1.0 lb ai/A), because residues of lactofen and all metabolites following application at 1.5x were below the LOQ (<0.01 ppm each) in/on all samples of tomatoes from the remaining two trials, these trials are acceptable.

Samples from the 2003 field trials were not analyzed for the lactofen metabolites that are still under consideration for inclusion in the tolerance expression for crops harvested at PHIs <45 days. HED had previously indicated that this decision would be revisited for any future registrations with PHIs of less than 45 days. Because residues of lactofen and all metabolites were below the LOQ in all samples analyzed from the 1990 and 1991 field trials, and provided these results are confirmed in the additional field trials required below, HED believes that the current tolerance of lactofen *per se* will be acceptable for tolerances resulting from the proposed use of lactofen on fruiting vegetables.

No crop field trial data were submitted to support the proposed use on okra. Okra will be added to the fruiting vegetable crop group (Personal communication, B. Schneider 10/13/06), so the tomato and pepper data may be translated to okra.

Geographic representation is inadequate for the fruiting vegetables crop group. The petitioner has proposed use in Zones 2, 3, and 4; however, only data from Zone 3 were submitted. Due to the lack of detectable residues, and that Zones 2 and 4 are adjacent to Zone 3, no additional data are required to support the requested tolerance. The available field trial data for pepper and tomato indicate that residues will not exceed the proposed tolerance for residues of lactofen *per se* in/on the fruiting vegetables crop group 8 and okra at 0.02 ppm.

If the petitioner wishes to pursue a national section 3 registration in the future, then at least one of the additional tomato field trials must reflect application to a tomato variety that bears small fruit.

860.1520 Processed Food and Feed

A processing study is not required for tomatoes because no detectable residues were observed in tomatoes following treatment at 5x the maximum proposed application rate (~5 lb ai/A).

860.1650 Submittal of Analytical Reference Standards

Analytical standards for lactofen, its metabolites PPG-947, PPG-1576, and PPG-2597, and the internal standard PPG-1530 are currently available in the National Pesticide Standards Repository (personal communication with D. Wright, 7/17/06). Although a standard for metabolite PPG-847 has not been submitted, because the current tolerance expression for lactofen is restricted to lactofen *per se*, and because the submitted crop field trial data suggest that the current tolerance expression is appropriate for the proposed use on fruiting vegetables, a standard for PPG-847 is not required at this time.

860.1850 Confined Accumulation in Rotational Crops

D263857, 5/4/00, C. Olinger
D222025 and D285906, 7/21/04, N. Dodd

An acceptable confined rotational crop study in root crops indicated that there was minimal uptake of radioactivity in carrots and radishes planted between 42 and 119 days after treatment of soil with [^{14}C]lactofen.

A confirmatory study was conducted on lettuce, carrots, radish and wheat, which indicated that total radioactive residues (TRR) were <0.02 ppm in all rotational crops except wheat grain (0.10 ppm), forage (0.12 ppm), and straw (0.27 ppm). Residues in wheat grain were not characterized/identified. Residues in wheat forage and straw were extracted with methanol and analyzed by GC/ECD. Lactofen *per se* was not detected (<0.05 ppm) in either wheat forage or straw, and no metabolites were identified.

Additional storage stability information/data were required for the confirmatory study; however, it was concluded that, pending receipt of storage stability data, the study would be adequate to indicate that residues of lactofen *per se* will not occur in rotational crops planted in soil treated with lactofen at the rate of 0.92 lb ai/A (~1x the maximum proposed seasonal rate for fruiting vegetables) at plantback intervals of 72 days for wheat, 221 days for radish, or 291 days for carrots and lettuce.

860.1900 Field Accumulation in Rotational Crops

EAB Memo, 9/30/86, S. Simko
D222025 and D285906, 7/21/04, N. Dodd

A field rotational crop study was previously reviewed by EAB. Lactofen (2 lb/gal EC) was applied to silt loam and loam soils located in OH, MN, and MO at 0.25-1.0 lb ai/A. The plantback intervals were 1-339 days for wheat, 55-368 days for lettuce, and 55-368 days for radishes. Residues of lactofen and metabolites PPG-847, PPG-947, PPG-1576, and PPG-2053 (not a residue of concern) were <0.05 ppm in wheat planted >1 day, radishes planted >35 days, and lettuce planted >55 days following application of the 2 lb/gal EC formulation at 0.25-1.0 lb ai/A.

Additional data pertaining to the field conditions and the analytical method for PPG-2053 were required for the field rotational crop studies; however, HED concluded that the available confined and field rotational crop data on wheat (a grain crop), lettuce (a leafy vegetable), and radish/carrot (root crops) are adequate to indicate that residues of lactofen *per se* are not taken up by rotational crops after soil is treated at up to 0.50 lb ai/A (0.5x the maximum seasonal rate for fruiting vegetables). In support of proposed uses on cotton and peanut, HED previously concluded that no rotational crop restriction was needed based on reported residues of lactofen *per se* in treated crops (<0.01 ppm in snap bean, cottonseed, soybean, peanut, and, with one exception, in cotton gin byproducts).

Conclusions. The available confined rotational and field rotational crop data, though inadequate, are sufficient to indicate that plantback restrictions are not required for the proposed use of lactofen on fruiting vegetables.

860.1550 Proposed Tolerances

Current tolerances [40 CFR §180.432(a)] for lactofen in/on plant commodities are expressed in terms of the herbicide lactofen, 1-(carboethoxy)ethyl 5-[2-chloro-4-(trifluoromethyl)phenoxy]-2-nitrobenzoate.

There are no established or proposed Codex, Canadian, or Mexican MRLs for residues of lactofen in any crop. Therefore, there are no harmonization issues with respect to U.S. tolerances.

In support of the proposed uses on the fruiting vegetables crop group 8 and okra, the petitioner has proposed to establish tolerances for the residues of lactofen and its associated metabolites containing the diphenyl ether linkage expressed as lactofen in/on the fruiting vegetables crop group and okra at 0.01 ppm for each crop. The proposed tolerances are presented in Table 5.

Acceptable field trial data for the fruiting vegetables crop group were submitted. The available field trial data will support tolerances with a regional registration for residues of lactofen *per se* in/on the fruiting vegetables crop group and okra at 0.02 ppm.

The proposed tolerances for the fruiting vegetables crop group and okra should be revised to reflect the recommended tolerance expression and the correct commodity definition as specified in Table 5.

We note that the Tolerance Assessment Spreadsheet was not used to calculate the proposed tolerance for fruiting vegetables and okra because residues were below the limit of quantitation in/on all samples.

Table 5. Tolerance Summary for Lactofen

Commodity	Proposed Tolerance (ppm)	Recommended Tolerance (ppm)	Comments; *Correct Commodity Definition*
Vegetable, fruiting, group	0.01	0.02	*Vegetable, fruiting, group 8*
Okra	0.01	0.02	

References

DP Barcode: None
Subject: EAB. Rotational Crop Review
From: J. Simko
To: S. Creeger
Date: 9/30/86
MRIDs: Acc. Nos. 071228 and 071228

DP Barcode: RD D241826
Subject: TGAI Product Chemistry Review/Action: 345. Reg. File Symbol No.: 59639-94. Chemical: Lactofen—76.7% pure. Company: Valent U.S.A. Corp.
From: H. Podall
To: S. Stanton
Date: 1/16/98
MRIDs: 44447001-44447003

DP Barcode: RD D242241
Subject: Product Chemistry Review of TGAI. Reg./File Symbol No.: 59639-94. Product Name: Lactofen Technical.
From: S. Mathur
To: J. Miller
Date: 2/5/98
MRIDs: 44460901-44460903

DP Barcode: D265469
Subject: Lactofen: HED Metabolism Assessment Review Committee Decision Memorandum; Chemical No. 128888.
From: C. Olinger and E. Mendez
To: G. Kramer
Date: 4/26/00
MRIDs: None

DP Barcode: D263857
Subject: Tolerance Reassessment of Lactofen: Product and Residue Chemistry Considerations; PC Code: 128888.
From: C. Olinger
To: S. Stanton and C. Scheltema
Date: 5/4/00
MRIDs: None

DP Barcode: None
Subject: Lactofen - Report of the Cancer Assessment Review Committee
From: S. Diwan
To: R. Fricke
Date: 5/22/02
MRIDs: None

DP Barcode: D222025 and D285906
Subject: Lactofen. Registration for Use on Cotton and Peanut. Summary of Analytical Chemistry and Residue Data. Petition Numbers 9F03798 (Cotton) and 8F03591 (Peanut).
From: N. Dodd
To: J. Miller/J. Stone
Date: 7/21/04
MRIDs: 00117578, 43871501, 43871502, 43871503, 44156102, 44156103, and 44156104

Attachments:
International Residue Limit Status sheet

Template Version September 2005

INTERNATIONAL RESIDUE LIMIT STATUS

Chemical Name: 1-(carboethoxy)ethyl 5-[2-chloro-4-(trifluoromethyl)phenoxy]-2-nitrobenzoate	Common Name: Lactofen	X Proposed tolerance □ Reevaluated tolerance □ Other	Date: 06/17/06

Codex Status (Maximum Residue Limits)	U. S. Tolerances
√ No Codex proposal step 6 or above □ No Codex proposal step 6 or above for the crops requested	Petition Number: PP#5E6930 DP Barcode: D356302 Other Identifier:
Residue definition (step 8/CXL): N/A	Reviewer/Branch: L. Cheng (RAB3)
	Residue definition: Lactofen *per se*

Crop (s)	MRL (mg/kg)	Crop(s)	Tolerance (ppm)
		Vegetable, fruiting, group	0.01
		Okra	0.01

Limits for Canada	Limits for Mexico
√ No Limits □ No Limits for the crops requested	√ No Limits □ No Limits for the crops requested
Residue definition: N/A	Residue definition: N/A

Crop(s)	MRL (mg/kg)	Crop(s)	MRL (mg/kg)

Notes/Special Instructions:
S. Funk, Jul 17, 2006.