



Clothianidin/66330-40 & 66330-52/PC Code 044309/Arvesta Corporation/66330
 DACO 7.4.1/OPPTS 860.1500/OECD IIA 6.3.1, 6.3.2, 6.3.3 and IIIA 8.3.1, 8.3.2, 8.3.3
 Processed Food and Feed - Potato (Granules, Chips, and Wet Peels)

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 RAB2/HED (7509C)

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This DER was originally prepared under contract by Dynamac Corporation (1910 Sedwick Road, Building 100, Suite B, Durham, NC 27713). It has been reviewed by HED and revised to reflect current OPP policies.

STUDY REPORT

MRID #46357302. Sandra J. Carringer (2003) *Magnitude of the Residue of TM-444 and its Metabolite in Potato Raw Agricultural and Processed Commodities*. Study #TCI-03-075. Unpublished study prepared by Arvesta Corporation, Morse Laboratories Incorporated, and The National Food Laboratory Incorporated. 420 pages. {OPPTS Residue Chemistry Test Guideline 860.1500}

EXECUTIVE SUMMARY

In two processing studies conducted in Idaho during 2003, clothianidin was applied to potatoes in side-by-side tests using water-dispersible granule (WDG) and water-soluble granule (WSG) formulations. The Belay™ 16WSG formulation was applied to potatoes as a single in-furrow application (to soil) at a rate of 0.986 pounds of active ingredient per acre (lb ai/A) at planting (roughly 5X the proposed maximum seasonal use rate of 0.2 lb ai/A). The Clutch™ 50WDG formulation was applied during tuber development as three foliar broadcast applications at a rate of 0.333 to 0.337 lb ai/A per application, with re-treatment intervals (RTIs) of 7 days, for a total use rate of 1.01 lb ai/A per season (roughly 7X the proposed maximum seasonal use rate of 0.14 lb ai/A). Potato tubers were harvested at commercial maturity, 124 days after treatment (DAT) for the Belay™ 16WSG in-furrow applications and 14 DAT for the Clutch™ 50WDG foliar applications (14 days following the third treatment). Duplicate subsamples of potato tubers, the raw agricultural commodity (RAC), were collected and the remaining bulk samples were processed into granules, chips, and wet peel using simulated commercial procedures. Prior to analysis, whole tubers (RAC) and samples of each processed fraction were stored frozen for up to 17 days, a duration supported by available storage stability data.

The LC/MS/MS method (Morse Method #Meth-164) used to determine residues of clothianidin and its metabolite, TMG, in potato tubers and processed fractions was adequately validated in conjunction with the processing study. Residues in tubers, granules, and wet peel are extracted with acetonitrile/water/guanidine-HCl (20:80:1 vol/vol/wt), while residues in chips are extracted with acetonitrile/water/acetic acid/guanidine-HCl (20:80:0.1:1 vol/vol/vol/wt). The extracts are filtered and concentrated. Residues of clothianidin and TMG are then cleaned up separately using a ChemElut™ liquid/liquid extraction (LLE) or ENVI-Carb™ solid phase extraction (SPE) columns, respectively. Residues are concentrated, reconstituted in 1% acetic acid, and analyzed by LC/MS/MS. For each analyte, the validated limits of quantitation (LOQs) are 0.040 ppm (for chips) and 0.020 ppm (for tubers, granules/flakes, and wet peel). The limits of detection (LODs) are 0.013 ppm (for chips) and 0.007 ppm (for potato tubers, granules/flakes, and wet peel).

Residues of the metabolite, TMG, were non-detectable (less than 0.007 ppm) in all samples of tubers and processed commodities from both trials using either treatment regime. For



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 Processed Food and Feed - Potato (Granules, Chips, and Wet Peels).

the test using the Belay™ 16WSG formulation, residues of clothianidin averaged 0.026 ppm in tubers, 0.055 ppm in granules, 0.034 ppm (less than the LOQ) in chips, and 0.007 ppm (less than the LOQ) in wet peel. For the test using the Clutch™ 50WDG formulation, residues of clothianidin averaged 0.012 ppm (less than the LOQ) in tubers, 0.032 ppm in granules, 0.018 ppm (less than the LOQ) in chips, and 0.008 ppm (less than the LOQ) in wet peel.

The calculated processing factors for each matrix were similar regardless of the treatment regime. Average processing factors were 2.3X for granules/flakes, 1.4X for chips and 0.5X for wet peel.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS

Under the conditions and parameters used in the study, the potato processing data are classified as scientifically acceptable. The acceptability of this study for regulatory purposes is addressed in the forthcoming US EPA Residue Chemistry Summary Document (DP Barcodes D309473 and D309474).

COMPLIANCE

Signed and dated GLP, quality assurance, and data confidentiality statements were provided. No deviations from regulatory requirements were noted that would impact the study results or their interpretation.

A. BACKGROUND INFORMATION

Clothianidin (also known by its development code numbers, TM-444, TI-435, or V-10066) is a systemic insecticide, belonging to the chloronicotinyl (and nitroguanidine) class of chemicals, which enters the transpiration stream through the roots and cotyledons of newly germinating seedlings and protects below- and above-ground plant parts from insect damage. It binds (via ingestion and contact routes) with the nicotinic acetylcholine receptor sites, interfering with transmission of stimuli and eventually inhibiting reproduction of the insect. Clothianidin is a major metabolite of thiamethoxam. It is currently registered (40CFR §180.586) for use on various crops.

Arvesta has submitted a petition (PP#4F6869) requesting the establishment of tolerances for residues of clothianidin in/on grape and potato commodities. The 50% ai water-dispersible granule (WDG) formulation is proposed for foliar applications to grapes and potatoes (Clutch™ 50WDG, EPA Registration #66330-40). The 16% ai water-soluble granule (WSG) formulation is proposed for soil applications to grapes and potatoes (Belay™ 16WSG, EPA Registration #66330-52).

TABLE A.1 Nomenclature of Test Compound and its Metabolite.	
Compound	
Empirical Formula	C ₆ H ₈ ClN ₃ O ₂ S



TABLE A.1 Nomenclature of Test Compound and its Metabolite.

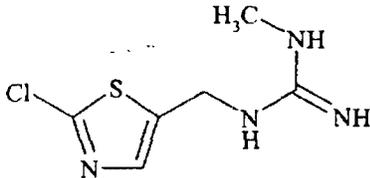
Common Name	Clothianidin
Company Experimental Names	TM-444, TI-435, V-10066
IUPAC Name	(E)-1-(2-Chloro-1,3-thiazol-5-ylmethyl)-3-methyl-2-nitroguanidine
CAS Name	[C(E)]-N-[(2-Chloro-5-thiazolyl)methyl]-N'-methyl-N''-nitroguanidine
CAS Number	210880-92-5 (formerly 205510-53-8)
Chemical Class	Chloronicotinyl
Known Impurities of Concern	None
End-Use Product (EUP)	Clutch™ 50WDG, EPA Registration #66330-40 Belay™ 16WSG, EPA Registration #66330-52
Metabolite	
Common Name	Metabolite TMG
Company Experimental Name	TMG
CAS Name	[C(E)]-N-[(2-Chloro-5-thiazolyl)methyl]-N'-methylguanidine

TABLE A.2 Physicochemical Properties (from MRID #45422301).

Parameter	Value
Molecular Weight	249.7
Melting Point (°C)	176.8
pH at 23°C	6.24 [1% solution/suspension]
Density (g/cm ³) at 20°C	1.61 [PAI], 1.59 [TGAI]
Water Solubility (g/L) at 20°C	0.327
Solvent Solubility (g/L) at 25°C	n-Heptane <0.00104 Xylene 0.0128 1-Octanol 0.938 Dichloromethane 1.32 Ethyl Acetate 2.03 Methanol 6.26 Acetone 15.2
Vapor Pressure (Pa) at 25°C	1.3 x 10 ⁻¹⁰
Dissociation Constant (pK _a) at 20°C	11.09
Octanol/Water Partition Coefficient (Log K _{ow}) at 25°C	0.7
UV/Visible Absorption Spectrum, Maximum (nm)	265.5 [acidic, neutral sol'ns]. 246.0 [basic sol'n].

B. EXPERIMENTAL DESIGN

B.1. Application and Crop Information

The Clutch™ 50WDG and Belay™ 16WSG formulations were compared using side-by-side treatments conducted in 2003 (see Table B.1). Clothianidin, formulated as Clutch™



50WDG, was applied as three foliar broadcast applications at a rate of 0.333 to 0.337 lb ai/A per application, with an RTI of 7 days, during tuber development. The total application rate for the foliar broadcast treatment was 1.01 lb ai/A per season (roughly 7X the proposed maximum seasonal use rate of 0.14 lb ai/A). The Belay™ 16WSG formulation treatment was a single in-furrow application at a rate of 0.986 lb ai/A (roughly 5X the proposed maximum seasonal use rate of 0.2 lb ai/A). Potato tubers were harvested at commercial maturity, 124 DAT for the Belay™ 16WSG treatment, and 14 DAT for the Clutch™ 50WDG treatment (14 days following the third treatment).

Location (City, State/Year)	Application						
	EUP	Method ¹ ; Timing ²	Volume (GPA) ³	Single Rate ⁴ (lb ai/A)	Number	RTI (Days)	Total Rate (lb ai/A)
Payette, ID/2003	Belay™ 16WSG	In-furrow; at planting.	15	0.986	1	NA ⁵	0.986
	Clutch™ 50WDG	Foliar broadcast; tuber development.	30-31	0.333- 0.337	3	7	1.01

1. All applications were made using ground equipment. No tank mix adjuvants were used for any applications.
2. The first (or only) applications were made from planting to tuber development, depending upon treatment regime.
3. GPA = Gallons Per Acre.
4. The target single application rate was 0.99 lb ai/A for the in-furrow treatment, and 0.331 lb ai/A for the foliar treatment. The target total application rate was 0.99 lb ai/A for both treatment regimes.
5. NA = Not Applicable.

B.2. Processing Procedures

After collection, bulk samples of potato tubers (87 to 90 lbs each) were shipped at ambient temperatures to The National Food Laboratory in Dublin, California, and placed in cool storage (70 ± 5°F) prior to processing. A single control and duplicate treated samples of potato tubers (RAC) were collected and the remaining bulk samples were processed into granules, chips and wet peel (duplicate samples from each treatment) using simulated commercial procedures. All samples were then placed in frozen storage (10 to 24°F). All samples were then shipped frozen by freezer truck to the analytical laboratory, Morse Laboratories in Sacramento, California, and placed in frozen storage (-20 ± 5°C). The RAC, wet peel, and potato chip samples were homogenized prior to analysis.

B.3. Analytical Methodology

Residues of clothianidin and TMG were determined in potato tubers (RAC) and processed fractions using an LC/MS/MS method entitled *Determination of TM-444 and TMG in Grape and Potato Raw Agricultural and Processed Commodities* (Morse Method #Meth-164). A detailed description of Method #Meth-164 is presented in the DER for MRID #46346801, in conjunction with an independent laboratory validation (ILV) of that method.

With the exception of potato chips, residues of both clothianidin and TMG are extracted with acetonitrile/water/guanidine-HCl (20:80:1 vol/vol/wt) and filtered through Celite. For chips, residues are extracted with acetonitrile/water/acetic acid/guanidine-HCl (20:80:0.1:1 vol/vol/vol/wt) and filtered. The filtrate is concentrated and diluted with water. Separate aliquots are then taken for further cleanup and determination of clothianidin and TMG. Residues



of clothianidin are cleaned up using a ChemElut™ LLE column eluted with cyclohexane/ethyl acetate (1:1 vol/vol). Residues of TMG are cleaned up using a ENVI-Carb™ SPE cartridge eluted with methanol/water/acetic acid (80:20:1 vol/vol/vol). The purified residues are concentrated and re-dissolved in 1% acetic acid for separate determination by LC/MS/MS. The HPLC system consists of a C₁₈ column with a mobile phase gradient of water to methanol, each containing 1% formic acid. The retention times for clothianidin and TMG are approximately 7.3 and 4.5 minutes, respectively. The monitored transitions are m/z 250 to 169 for clothianidin and m/z 205 to 132 for TMG. The validated LOQs for clothianidin residues are 0.040 ppm (for potato chips) and 0.020 ppm (for potato tubers, granules/flakes, and wet peel). The LODs are 0.013 ppm (for potato chips) and 0.007 ppm (for potato tubers, granules/flakes, and wet peel).

C. RESULTS AND DISCUSSION

Samples were stored frozen from collection to analysis for durations of up to 17 days (see Table C.2). Storage stability data (MRID #46357301) are available for potato tubers indicating that clothianidin is stable in frozen storage for intervals of up to 6 months. These data will support the current potato processing study.

The LC/MS/MS method (Morse Method #Meth-164) used to determine clothianidin residues in potato tubers, granules/flakes, chips, and wet peel is adequate for data collection. Method validation recoveries for clothianidin were 75 to 92% from all potato matrices with standard deviations of ± 7 to 14% (see Table C.1). The metabolite TMG recoveries were 77 to 96% from all potato matrices with standard deviations of ± 5 to 11%. Apparent residues of clothianidin and TMG were less than the LOD in all control samples.

In a trial conducted in Idaho during 2003, the Clutch™ 50WDG and Belay™ 16WSG formulations were compared using side-by-side treatments. In one test, clothianidin (as Clutch™ 50WDG) was applied (during tuber development) as three foliar broadcast applications at a rate of 0.333 to 0.337 lb ai/A per application, with RTIs of 7 days, for a total use rate of 1.01 lb ai/A per season (7X). In the other test, clothianidin (as Belay™ 16WSG) was applied (at planting) as a single in-furrow application at a rate of 0.986 lb ai/A (5X). Potato tubers were harvested at commercial maturity, 124 DAT for the Belay™ 16WSG treatment and 14 DAT for the Clutch™ 50WDG treatment. Duplicate subsamples of potato tuber (RAC), granules/flakes, chips, and wet peel were collected.

Residues of clothianidin in tubers averaged 0.026 ppm following the 5X early season application of the Belay™ 16WSG formulation and 0.012 ppm (less than the LOQ) following the 7X foliar applications of the Clutch™ 50WDG formulation (see Table C.3). Residues of TMG were not detected in whole tubers or in any of the processed fractions. For the Belay™ 16WSG and Clutch™ 50WDG formulations, residues of clothianidin averaged (respectively) 0.055 and 0.032 ppm in granules, 0.034 and 0.018 ppm in chips, and 0.007 and 0.008 ppm in wet peel. Although clothianidin residues were less than the LOQ in chips and wet peel, residue were greater than the LOD and were therefore used to estimate processing factors.

The calculated processing factors for each matrix were similar regardless of the treatment regime. The processing factors were 2.1X and 2.6X for granules/flakes, 1.3X and 1.5X for chips, and 0.3X and 0.7X for wet peel.



TABLE C.1 Method Validation Recovery Results for the LC/MS/MS Method from Potato Matrices.

Analyte	Potato Matrix	Spiking Level (mg/kg)	Sample Size	Clothianidin	
				Recoveries (%)	Mean Recovery ± Std Dev (%)
Clothianidin	Tuber [RAC]	0.020	3	83-96	86 ± 8
		0.500	3	79-82	
	Granule/Flake	0.020	3	61-81	75 ± 7
		0.500	3	76-78	
	Chip	0.040	3	70-76	78 ± 7
		1.00	3	81-87	
Wet Peel	0.020	3	85-119	92 ± 14	
	0.500	3	82-90		
TMG	Tuber [RAC]	0.020	3	87-113	96 ± 11
		0.500	3	83-100	
	Granule/Flake	0.020	3	72-76	77 ± 5
		0.500	3	79-83	
	Chip	0.040	3	90-103	93 ± 6
		1.00	3	86-96	
Wet Peel	0.020	3	87-106	93 ± 10	
	0.500	3	82-103		

TABLE C.2 Summary of Freezer Storage Conditions.

Potato Matrix	Storage Temperature (°C)	Actual Storage Duration (Days) ¹	Limit of Demonstrated Storage Stability (Months) ²
Tuber, Granule, Chip, Wet Peel	-20 ± 5	11-17	6

1. Extracts were stored frozen for up to 6 days prior to analysis.
2. Storage stability data are available indicating that clothianidin is stable under frozen conditions in potato tuber for up to 6 months (MRID #46357301).

TABLE C.3 Residue Data from Potato Processing Study with Clothianidin.

Trial ID (City, State/Year)	Potato Processed Commodity	Treatment	Total Rate (lb ai/A)	PHI (Days)	Residues (ppm) ¹		Processing Factor ³
					Clothianidin ²	TMG	
Payette, ID/2003	Tuber [RAC]	In-furrow	0.986	124	0.030, 0.021 [0.026]	ND ⁴	NA ⁵
		Foliar	1.01	14	0.013, 0.011 [0.012]	ND	NA
	Granules/Flakes	In-furrow	0.986	124	0.051, 0.058 [0.055]	ND	2.1
		Foliar	1.01	14	0.033, 0.031 [0.032]	ND	2.6
	Chips	In-furrow	0.986	124	0.029, 0.039 [0.034]	ND	1.3
		Foliar	1.01	14	0.019, 0.017 [0.018]	ND	1.5



Trial ID (City, State/Year)	Potato Processed Commodity	Treatment	Total Rate (lb ai/A)	PHI (Days)	Residues (ppm) ¹		Processing Factor ³
					Clothianidin ²	TMG	
	Wet Peel	In-furrow	0.986	124	<i>0.007, 0.007</i> [0.007]	ND	0.3
		Foliar	1.01	14	<i>0.007, 0.008</i> [0.008]	ND	0.7

1. For each analyte, the LOQ is 0.040 ppm (potato chips), and 0.020 ppm (potato tubers, granules/flakes, and wet peel). The LOD is 0.013 ppm (potato chips), and 0.007 ppm (potato tubers, granules/flakes, and wet peel).
2. Residue values in *italics* are between the LOD and the LOQ [average residues are presented in brackets].
3. The processing factor was calculated using the average residues of Clothianidin only in the potato RAC and processed fractions.
4. ND = Not detected (less than the LOD).
5. NA = Not Applicable.

D. CONCLUSION

The potato processing data are adequate and indicate that there is the potential for the concentration of clothianidin residues in granules/flakes and chips. Processing factors for the various matrices were similar between the two treatment regimes; average processing factors were 2.3X for granules/flakes, 1.4X for chips, and 0.5X for wet peel.

E. REFERENCES

Subject: *Independent Laboratory Validation for the Determination of TM-444 and TMG in Grapes*, Laboratory Study ID #Arvesta-1506

Author: Diane E. Reed

Dated: 2004

MRID: 46346801

F. DOCUMENT TRACKING

RDI: W. T. Drew (8/29/2005), R. A. Loranger (12/28/2005)

Petition Number: P2F6445

DP Barcode: D309473 and D309474

PC Code: 128831



13544



R126701

Chemical: Clothianidin

PC Code:
044309

HED File Code: 11000 Chemistry Reviews

Memo Date: 12/28/2005

File ID: DPD309473

DPD309474

Accession #: 412-06-0194

HED Records Reference Center
7/27/2006

