VOLUME ___ OF ___ OF SUBMISSION

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Profenofos/Lambda-Cyhalothrin

Polytrin KA 315 EC/ULV (A13735F) - Skin Sensitisation Study in the Guinea Pig

Final Report

DATA REQUIREMENTS: EPA Health Effects Test Guidelines, OPPTS 870.2600 (1998)
OECD Guidelines for Testing of Chemicals, Procedure 406 (1992)

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STUDY COMPLETION DATE: October 7, 2003

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LABORATORY PROJECT ID: Report Number: CTL/GG7732/Regulatory/Report
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Task Number: T008649-07

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VOLUME 1 OF 1 OF STUDY

STATEMENTS OF DATA CONFIDENTIALITY CLAIMS

1) *The following statement applies to submissions to regulatory agencies in the United States of America.*

STATEMENT OF NO DATA CONFIDENTIALITY CLAIM

No claim of confidentiality is made for any information contained in this study on the basis of its falling within the scope of FIFRA Section 10 (d) (1) (A), (B), or (C).

Company: Syngenta Crop Protection, Inc.

Company Representative: Timothy E. Wilson, Ph.D.

Title: Regulatory Product Manager

Signature: Timothy E Wilson Date: Jan. 10, 2008

These data are the property of Syngenta Crop Protection, Inc. and, as such, are considered to be confidential for all purposes other than compliance with the regulations implementing FIFRA Section 10.

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STATEMENT OF GLP COMPLIANCE AND AUTHENTICATION

I, the undersigned, declare that the objectives laid down in the protocol were achieved and that the data generated are valid. The report fully and accurately reflects the procedures used and the raw data generated in the above study.

The study (GG7732) was conducted in compliance with the UK Principles of Good Laboratory Practice (The United Kingdom GLP Regulations 1999, Statutory Instrument No. 3106) except for the deviation listed below. These Principles are in accordance with the OECD Principles of Good Laboratory Practice, revised 1997 (ENV/MC/CHEM(98)17).

The following GLP deviation is considered not to affect the integrity of the study or the validity of the conclusions drawn:

(i) the stability, homogeneity and achieved concentration of the test substance in the vehicle used were not determined by analysis.

I R Johnson
Study Director

..... 7 October 2003
Date

Merrill Tisdel, B.S.
Representative of Submitter/Sponsor

Date

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This page
may be required
by some
regulatory authorities.

NOT APPLICABLE

QUALITY ASSURANCE STATEMENT

In accordance with CTL policy and QA procedures for Good Laboratory Practice, this report has been audited and the conduct of this study has been inspected as follows:

Date	Audit/Inspection	Date of QA Report
13 Sep 2003	Draft report	15 Sep 2003
06 Oct 2003	Final report review	06 Oct 2003

In addition, inspections associated with this type of study were made as follows:

15 Apr 2003	Protocol	15 Apr 2003
28 May 2003	Dose preparation	28 May 2003
29 May 2003	Topical application	29 May 2003
30 May 2003	Assessment	02 Jun 2003
30 Jun 2003	Decontamination, site identification	01 Jul 2003

Facilities and process based procedures associated with this type of study were inspected in accordance with QA Standard Operating Procedures.

So far as can be reasonably established, the methods described and the results given in the final report accurately reflect the raw data produced during the study, GG7732.

I F Bayliss ..... 7 October 2003

(CTL Quality Assurance Unit)

STUDY CONTRIBUTORS

The following contributed to this report in the capacities indicated:

Name	Title
I R Johnson	Study Director
S Buttle	Study Licensee
D Lees	Study Reviewer
A M Leah	Report preparation

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APPENDICES

1. SUMMARY

1.1 Study design

The sensitisation potential of POLYTRIN KA 315 EC/ULV (A-13735 F) was assessed using a method based on that described by Ritz and Buehler (1980). The study involved the treatment of guinea pigs using two procedures: the potential induction of an immune response and a challenge of that response.

The sensitisation response of the animals was determined 1 and 2 days after challenge by assessing the degree of erythema.

1.2 Results

Challenge of previously-induced guinea pigs with the undiluted test substance elicited an erythematous response which was similar in test and control animals

Challenge of previously-induced guinea pigs with a 75% w/v preparation of the test substance in deionised water elicited a net response of 34%.

Rechallenge with a 50% or a 25% w/v preparation of the test substance in deionised water elicited a small response which was greater in control animals than in test animals.

A positive control study using hexylcinnamaldehyde demonstrated the sensitivity of the test system.

1.3 Conclusion

Based on the results of this study, POLYTRIN KA 315 EC/ULV (A-13735 F) is considered to be a skin sensitiser in the guinea pig.

According to Commission Directive 2001/59/EC, POLYTRIN KA 315 EC/ULV (A-13735 F) is considered to be a skin sensitiser in the guinea pig and a classification is required (R43, may cause sensitisation by skin contact).

2. INTRODUCTION

2.1 Purpose

The purpose of this study was to assess the skin sensitisation potential of POLYTRIN KA 315 EC/ULV (A-13735 F) in the guinea pig.

2.2 Regulatory guidelines

This study was conducted in accordance with the following Regulatory Guidelines:

a) OECD guideline reference 406 (1992) : Skin sensitisation.

b) Annex V to Council Directive 67/548/EEC on the approximation of laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances, published in the Twenty second Adaptation, Commission Directive 96/54/EC, OJEC L248, 206-212, 1996. (B.6 : Skin sensitisation).

c) United States Environmental Protection Agency, Health Effects Test Guidelines, OPPTS 870.2600 (1998): Skin Sensitisation.

2.3 Justification for test system selection

The albino guinea pig was used because it is the species generally recommended for the assessment of skin sensitisation potential. The Dunkin Hartley strain of guinea pig was used because of the substantial background data available for this strain, in this Laboratory, relating to studies of this type. In addition, the test system has been shown to respond to a positive control substance (see Section 2.5). The Buehler method was chosen as the dermal route represents a likely route of exposure to man.

2.4 Dose level selection

The dose levels selected for the induction and challenge stages of this study were determined by a sighting phase in the guinea pig. This is reported in Appendix A.

2.5 Positive control study

The reliability of the test system is assessed at approximately 6-monthly intervals using a known sensitiser (hexylcinnamaldehyde). The positive control study closest in time to the main study is reported in Appendix B.

2.6 Study dates

The main study was initiated on 4 June 2003. The experimental phase started on 11 June 2003 and was completed on 9 August 2003. For the positive control study, the experimental phase started on 30 April 2003 and was completed on 31 May 2003.

2.7 Data storage

An original report, the study protocol and all raw data, samples and specimens, pertaining to this study (and the raw data for the positive control study) are retained in the Archives, Central Toxicology Laboratory (CTL), Alderley Park, Macclesfield, Cheshire, UK.

3. TEST AND CONTROL SUBSTANCES

3.1 Test substance

Name:	POLYTRIN KA 315 EC/ULV
Source:	Syngenta Crop Protection Münchwilen AG
Colour:	Yellow-orange
Physical state:	Liquid
Batch reference number:	SEZ3CP001
Formulation reference number:	A-13735 F
CTL test substance reference number:	Y03088/036
AI content of formulation (w/v):	CGA15324 - 30.2% Lambda-cyhalothrin – 1.56%
Expiry date:	July 2005
Storage conditions:	Ambient temperature in the dark

A certificate of analysis (dated 27 May 2003) is retained in the CTL Archives. The test substance was characterised by Syngenta Crop Protection Münchwilen AG.

3.2 Control substance/vehicle

The control substance and vehicle for the test substance was deionised water (CTL test substance reference: Y04517/015).

4. EXPERIMENTAL PROCEDURES

4.1 Dose preparations

All dose preparations were used within 24 hours of preparation. For each concentration, where appropriate, a measured amount of the test substance was added to a measured amount of deionised water and was mixed thoroughly.

No correction was made for the purity of the active ingredient in the test substance. Stability, homogeneity and achieved concentration were not determined.

4.1.1 Induction phase

The test substance was applied undiluted.

4.1.2 Challenge phase

The test substance was applied undiluted and as a 75% w/v preparations in deionised water for the first challenge and as 50% and 25% w/v preparations in deionised water for the second challenge.

4.2 Experimental design

4.2.1 Animals

Species:	Guinea pig
Strain:	Dunkin Hartley
Source:	David Hall, Newchurch, Burton-on-Trent, Staffs, UK. Harlan UK, Shaws Farm, Bicester, Oxfordshire (control animals for the rechallenge)
Sex:	Female
Number used:	Nineteen test and ten control (plus ten control for the rechallenge)
Age:	Young adults.
Weight range:	The animals weighed 255-303g at the beginning of the study. Control animals used for the rechallenge weighed 411-601g.

4.2.2 Accommodation and husbandry

The guinea pigs were housed five per cage in cages suitable for animals of this strain and the weight range expected during the course of the study.

The animal room was designed to give the environmental conditions shown below.

Temperature:	18±3°C
Relative humidity:	30-70%
Air changes:	A minimum of 15 changes/hour
Light cycle:	Artificial, giving 12 hours light, 12 hours dark

Both temperature and relative humidity were recorded daily. There was a slight variation in temperature (14-23°C) and an increase in relative humidity (maximum 89%) on a number of days, but this is considered to have had no detrimental effect on the scientific integrity of the study.

Diet (FD1), supplied by Special Diets Services, Witham, Essex, UK, and mains water, supplied by an automatic system, were available *ad libitum*.

Each batch of diet is routinely analysed for composition and for contaminants. Water is also periodically analysed for contaminants. No contaminants were found in the diet or water at levels considered likely to interfere with the purpose or outcome of the study. Certificates of analyses are retained in the CTL Archives.

4.2.3 Acclimatisation

The animals were housed under the experimental conditions for at least 5 days, prior to the start of dosing.

4.2.4 Animal identification

Animals were individually identified with a number, unique within the study, which was written on a small area of clipped flank, using a waterproof marker pen.

On the front of each cage was a card identifying the animals within.

4.3 Induction and challenge

4.3.1 Induction phase

An area approximately 5 x 5cm on the scapular region of each animal was clipped free of hair with a pair of veterinary clippers and treated with a topical application of either 0.4ml of the undiluted test substance (test group) or a dry dressing only (control group). The test substance was applied to a lint patch (approximate size 2 x 2cm). The lint patch was applied to the test area and covered with an occlusive dressing and adhesive elastic bandage, secured with PVC tape. This occlusive dressing was left in place for at least 6 hours.

The induction process was repeated at the same site during the next two weeks giving a total of three, 6-hour exposures. The interval between each exposure was 7 days. The irritation response was noted approximately 1 day after the removal of each patch and before application of the subsequent patch. The animals were clipped prior to each application.

The animals were left untreated for two weeks after the final induction exposure, prior to challenge.

4.3.2 Challenge phase

An area approximately 5 x 15cm on both flanks of each animal was clipped free of hair with a pair of veterinary clippers. An occlusive dressing was prepared which consisted of two lint patches (approximate size 1 x 2cm) stitched to a piece of rubber sheeting (approximate size 5 x 12cm).

Approximately 0.1-0.2ml of the undiluted test substance was applied to one lint patch and a similar volume of the 75% w/v preparation was applied to the second lint patch. The dressing was applied to the shorn flanks of the guinea pig so the undiluted test substance was on the left and the 75% w/v preparation was on the right. The dressing was held in place by adhesive, impermeable, polyethylene tape (approximate size 7.5 x 30cm). Test and control animals were treated identically.

The patches were left in position for at least 6 hours. The dressings were then cut using blunt-tipped scissors, removed and discarded. The positions of the application sites were identified using a black, waterproof marker pen.

Skin sites were examined 1 and 2 days after removal of the dressings.

The interpretation of the results was complicated by an irritancy reaction, and nine days after the initial challenge the animals were re-challenged using two concentrations: 50% and 25% w/v of the test substance. Both flanks were again clipped free of hair but the preparation was applied to different sites than those used for the initial challenge. A new group of 10 control guinea pigs was used for the re-challenge. The animals were killed when the results had been assessed.

4.4 Clinical observations

4.4.1 General observations

Prior to the start of the study, all guinea pigs were examined to ensure that they were physically normal and behaved normally. Throughout the study, the animals were observed daily. One test animal was killed on humane grounds just before the rechallenge. It was subsequently found to be pregnant. The data from this animal is, therefore, not reported.

4.4.2 Sensitisation response

Following challenge, erythematous reactions were quantified and recorded, using the four-point scale shown below, 1 and 2 days after removal of the dressings.

Scale

0 - no reaction
1 - scattered mild redness
2 - moderate and diffuse redness
3 - intense redness and swelling

4.5 Bodyweights

The animals were weighed on the day before dosing (day -1) and at the end of the study. The new control group for the re-challenge was weighed at the beginning and end of this procedure. Individual bodyweights are presented in Appendix C.

4.6 Termination

All animals were killed by an appropriate method.

5. DATA EVALUATION

Sensitisation potential was expressed as a net percentage response. This was calculated by subtracting the percentage of animals with positive responses at challenge in the control group from the percentage of animals with positive responses at challenge in the test group.

6. RESULTS

6.1 Induction

Signs of skin irritation were seen in all the test animals during the induction phase. There were no signs of irritation in any of the control animals.

Induction responses are given in Table 1.

6.2 Challenge

One of the test animals had a distended abdomen and was killed following the first challenge.

Following challenge of previously-induced guinea pigs with the undiluted test substance, scattered mild redness was seen in ten of the nineteen test animals. Scattered mild redness or moderate and diffuse redness was seen in five of the ten control animals. The net response was 3%.

Following challenge of previously-induced guinea pigs with a 75% w/v preparation of the test substance in deionised water, scattered mild redness or moderate and diffuse redness was seen in fourteen of the nineteen test animals. Scattered mild redness was seen in four of the ten control animals. The net response was 34%.

Following rechallenge with a 50% w/v preparation of the test substance in deionised water, scattered mild redness was seen in one of the nineteen test animals and two of the ten control animals. The control response was therefore greater than the test response.

Following rechallenge with a 25% w/v preparation of the test substance in deionised water. there was no erythematous response in any of the test animals. Scattered mild redness was

seen in one of the ten control animals. The control response was therefore greater than the test response.

Challenge responses are given in Table 2.

7. CONCLUSION

Based on the results of this study, POLYTRIN KA 315 EC/ULV (A-13735 F) is considered to be a skin sensitiser in the guinea pig.

According to Commission Directive 2001/59/EC, POLYTRIN KA 315 EC/ULV (A-13735 F) is considered to be a skin sensitiser in the guinea pig and a classification is required (R43, may cause sensitisation by skin contact).

8. REFERENCES

Ritz H L and Buehler E V (1980). Planning, Conduct and Interpretation of Guinea Pig Sensitisation Patch Tests. In: Current Concepts in Cutaneous Toxicity, V A Drill and P Lazar (Eds), Academic Press, New York, pp 25-40.

Official Journal of the European Communities, Commission Directive 2001/59/EC (adapting to technical progress for the 28th time Council Directive 67/548/EEC), L 225 (21 August 2001).

GLOSSARY FOR ANIMAL DATA TABLES

NAD	no abnormalities detected
X:*A	test substance adhered [$]
N:*A	test substance no longer adhered [$]
S:E	slight erythema
N:E	erythema no longer present
S:D	slight desquamation
N:D	desquamation no longer present
S:O	slight oedema
N:O	oedema no longer present
S:S	slight scabbing
N:S	scabbing no longer present

[$] - in the absence of other clinical signs the sites were normal

TABLE 1 - INDUCTION RESPONSES

TEST ANIMALS

Animal Number	24 Hours After 1st Induction	Immediately Prior to 2nd Induction	24 Hours After 2nd Induction	Immediately Prior to 3rd Induction	24 Hours After 3rd Induction
331	X:*A	N:*A	X:*A	N:*A	X:*A
332	X:*A	N:*A	X:*A	N:*A	S:O S:E X:*A
333	NAD	NAD	S:E S:O X:*A	N:E S:O N:*A	S:O S:E X:*A
334	X:*A	N:*A	X:*A	N:*A	S:O S:E X:*A
336	X:*A	N:*A	X:*A	N:*A	S:E S:O X:*A
337	X:*A	N:*A	X:*A	N:*A	S:E X:*A
338	X:*A	N:*A S:D	S:D X:*A S:E S:O	S:D N:*A S:E S:O	S:D S:E S:O X:*A
339	X:*A	N:*A S:D S:O S:E	S:D S:O S:E X:*A	S:D S:O S:E N:*A	S:D S:O S:E X:*A
340	X:*A	N:*A S:S	N:S X:*A S:E S:O	N:*A S:E S:O	S:E S:O X:*A

TABLE 1 - INDUCTION RESPONSES

TEST ANIMALS

Animal Number	24 Hours After 1st Induction		Immediately Prior to 2nd Induction		24 Hours After 2nd Induction		Immediately Prior to 3rd Induction		24 Hours After 3rd Induction	
341	X:*A		N:*A		X:*A		N:*A		S:E	X:*A
342	X:*A S:O	S:E	N:*A S:O	N:E S:D	S:O S:E	S:D	S:O N:E	S:D	S:O X:*A	S:D
343	X:*A S:O	S:E	N:*A S:O	S:E S:D	S:E S:D	S:O	S:E S:D	S:O	S:E S:D X:*A	S:O S:S
344	X:*A		N:*A S:D	S:S	S:S S:E X:*A	S:D S:O	S:S N:E N:*A	S:D S:O	N:S S:O X:*A	S:D S:E
345	X:*A		N:*A S:O	S:D	S:D S:E	S:O X:*A	S:D S:E	S:O N:*A	S:D S:E	S:O X:*A
346	X:*A S:O	S:E	N:*A N:O	N:E	S:E X:*A	S:O	S:E N:*A	S:O	S:E X:*A	S:O
347	X:*A		N:*A		X:*A		N:*A		S:E X:*A	S:O
348	X:*A		N:*A S:E	S:D S:O	S:D S:O	S:E X:*A	S:D S:O	S:E N:*A	N:D S:O	S:E X:*A
349	X:*A S:O	S:E	N:*A N:O	N:E	X:*A		N:*A		S:E X:*A	S:O
350	X:*A		N:*A		S:E S:O	X:*A	S:E S:O	N:*A	S:E S:D	S:O X:*A

TABLE 1 - INDUCTION RESPONSES

CONTROL ANIMALS

Animal Number	24 Hours After 1st Induction	Immediately Prior to 2nd Induction	24 Hours After 2nd Induction	Immediately Prior to 3rd Induction	24 Hours After 3rd Induction
351	NAD	NAD	NAD	NAD	NAD
352	NAD	NAD	NAD	NAD	NAD
353	NAD	NAD	NAD	NAD	NAD
354	NAD	NAD	NAD	NAD	NAD
355	NAD	NAD	NAD	NAD	NAD
356	NAD	NAD	NAD	NAD	NAD
357	NAD	NAD	NAD	NAD	NAD
358	NAD	NAD	NAD	NAD	NAD
359	NAD	NAD	NAD	NAD	NAD
360	NAD	NAD	NAD	NAD	NAD

TABLE 2 - CHALLENGE RESPONSES

RESULTS:-

FIRST CHALLENGE

	ANIMAL	SEX	Y03088/036 undiluted TOP LEFT 24 HRS	Y03088/036 undiluted TOP LEFT 48 HRS	Y03088/036 75% w/v TOP RIGHT 24 HRS	Y03088/036 75% w/v TOP RIGHT 48 HRS
TEST:	331	F	1	0	1	0
	332	F	1	0	1	0
	333	F	0	0	2	0
	334	F	0	0	1	1
	336	F	1	0	1	0
	337	F	1	0	1	0
	338	F	1	0	1	0
	339	F	0	0	1	1
	340	F	1	0	1	0
	341	F	1	1	1	0
	342	F	0	0	1	0
	343	F	0	0	1	0
	344	F	1	0	1	0
	345	F	0	0	0	0
	346	F	0	0	0	0
	347	F	0	0	1	0
	348	F	1	0	0	0
	349	F	1	0	0	0
	350	F	0	0	0	0

0 - NO REACTION
1 - SCATTERED MILD REDNESS
2 - MODERATE AND DIFFUSE REDNESS
3 - INTENSE REDNESS AND SWELLING

TABLE 2 - CHALLENGE RESPONSES

RESULTS:-

FIRST CHALLENGE

	ANIMAL	SEX	Y03088/036 undiluted TOP LEFT 24 HRS	48 HRS	Y03088/036 75% w/v TOP RIGHT 24 HRS	48 HRS
CONTROL:	351	F	2	0	1	0
	352	F	1	0	0	0
	353	F	1	0	0	0
	354	F	0	2	0	0
	355	F	0	0	1	0
	356	F	1	0	1	0
	357	F	0	0	0	0
	358	F	0	0	0	0
	359	F	0	0	1	0
	360	F	0	0	0	0

0 - NO REACTION
1 - SCATTERED MILD REDNESS
2 - MODERATE AND DIFFUSE REDNESS
3 - INTENSE REDNESS AND SWELLING

TABLE 2 - CHALLENGE RESPONSES

RESULTS:-

SECOND CHALLENGE

	ANIMAL	SEX	Y03088/036 50% w/v TOP LEFT 24 HRS	Y03088/036 50% w/v TOP LEFT 48 HRS	Y03088/036 25% w/v TOP RIGHT 24 HRS	Y03088/036 25% w/v TOP RIGHT 48 HRS
TEST:	331	F	0	0	0	0
	332	F	0	0	0	0
	333	F	0	0	0	0
	334	F	0	0	0	0
	336	F	1	0	0	0
	337	F	0	0	0	0
	338	F	0	0	0	0
	339	F	0	0	0	0
	340	F	0	0	0	0
	341	F	0	0	0	0
	342	F	0	0	0	0
	343	F	0	0	0	0
	344	F	0	0	0	0
	345	F	0	0	0	0
	346	F	0	0	0	0
	347	F	0	0	0	0
	348	F	0	0	0	0
	349	F	0	0	0	0
	350	F	0	0	0	0

0 - NO REACTION
1 - SCATTERED MILD REDNESS
2 - MODERATE AND DIFFUSE REDNESS
3 - INTENSE REDNESS AND SWELLING

TABLE 2 - CHALLENGE RESPONSES

RESULTS:-

			SECOND CHALLENGE			
			Y03088/036 50% w/v TOP LEFT		Y03088/036 25% w/v TOP RIGHT	
	ANIMAL	SEX	24 HRS	48 HRS	24 HRS	48 HRS
CONTROL:	423	F	0	0	0	0
	424	F	1	0	0	0
	425	F	0	0	0	0
	426	F	0	0	0	0
	427	F	0	0	0	0
	428	F	1	1	1	1
	429	F	0	0	0	0
	430	F	0	0	0	0
	431	F	0	0	0	0
	432	F	0	0	0	0

0 - NO REACTION
1 - SCATTERED MILD REDNESS
2 - MODERATE AND DIFFUSE REDNESS
3 - INTENSE REDNESS AND SWELLING

APPENDIX A - SIGHTING PHASE

Two female guinea pigs were given a single application of the undiluted test substance and 75%, 50% and 25% w/v preparations of the test substance in deionised water, as described in Section 4.3.

In the main phase of the study, the undiluted test substance was used for the induction phase as it did not produce any irritation. For the challenge, the undiluted test substance and a 75% w/v preparations were chosen for the first challenge, as these were not expected to produce irritation.

APPENDIX A - SIGHTING PHASE

Animal number	Time after removal of dressings (hours)	Dose-level (w/v)			
		undiluted	75%	50%	25%
79	24	0	0	0	1
	48	0	0	0	0
80	24	0	0	0	0
	48	0	0	0	0

0 – no reaction
1 – scattered mild redness

APPENDIX B - POSITIVE CONTROL STUDY

Current CTL Study Number: GG7743

Postive control substance:	Hexylcinnamaldehyde
Source:	Aldrich Chemicals
Colour:	Yellow
Physical state:	Liquid
Batch reference	29,128-5
CTL test substance reference number:	Y07859/001
Purity (w/w):	85%
Storage conditions:	Refrigerated (under an inert gas)

The control substance and vehicle for the positive control substance was corn oil (CTL test substance reference number : Y00790/014

The sensitising potential of hexylcinnamaldehyde was assessed using a method essentially as described in Section 4.3. The test substance was applied undiluted for the induction phase and challenge phase.

Induction

The application sites of many of the test animals were stained yellow by the test substance during the induction phase, but this did not prevent the assessment of irritation.

Signs of slight skin irritation were seen in a few of the twenty test animals during the induction phase of the study. There were no signs of irritation in any of the control animals.

Challenge

Following challenge of previously-induced guinea pigs with the undiluted test substance, scattered mild redness was seen in four of the twenty test animals. There was no erythematous response in any of the control animals. The net percentage response was calculated to be 20% and hexylcinnamaldehyde was therefore considered to be a skin sensitiser under the conditions of the test.

The induction responses, challenge results and the bodyweight data are given in the following tables.

APPENDIX B - POSITIVE CONTROL STUDY: INDUCTION RESPONSES

TEST ANIMALS

Animal Number	24 Hours After 1st Induction	Immediately Prior to 2nd Induction	24 Hours After 2nd Induction	Immediately Prior to 3rd Induction	24 Hours After 3rd Induction
1	NAD	NAD	X:*A	N:*A	X:*A
2	NAD	NAD	NAD	NAD	X:*A
3	X:*A	N:*A	X:*A	N:*A	X:*A
4	NAD	NAD	X:*A	X:*A	X:*A
5	NAD	NAD	NAD	NAD	NAD
6	NAD	NAD	S:D S:E X:*A	S:D N:E X:*A	S:D X:*A
7	X:*A	N:*A S:D	N:D X:*A	N:*A	NAD
8	NAD	NAD	NAD	NAD	X:*A
9	NAD	NAD	X:*A	N:*A	NAD
10	X:*A	N:*A	X:*A	N:*A	X:*A

APPENDIX B - POSITIVE CONTROL STUDY: INDUCTION RESPONSES

TEST ANIMALS

Animal Number	24 Hours After 1st Induction	Immediately Prior to 2nd Induction	24 Hours After 2nd Induction	Immediately Prior to 3rd Induction	24 Hours After 3rd Induction
11	NAD	NAD	NAD	NAD	X:*A
12	NAD	NAD	NAD	NAD	NAD
13	X:*A	X:*A	X:*A	N:*A S:D	N:D X:*A
14	NAD	NAD	NAD	NAD	NAD
15	NAD	NAD	NAD	NAD	X:*A
16	X:*A	N:*A S:D	N:D	NAD	NAD
17	X:*A	N:*A S:D	N:D X:*A	N:*A	NAD
18	NAD	NAD	NAD	NAD	NAD
19	NAD	NAD	X:*A	N:*A	NAD
20	NAD	NAD	NAD	NAD	NAD

APPENDIX B - POSITIVE CONTROL STUDY: INDUCTION RESPONSES

CONTROL ANIMALS

Animal Number	24 Hours After 1st Induction	Immediately Prior to 2nd Induction	24 Hours After 2nd Induction	Immediately Prior to 3rd Induction	24 Hours After 3rd Induction
21	NAD	NAD	NAD	NAD	NAD
22	NAD	NAD	NAD	NAD	NAD
23	NAD	NAD	NAD	NAD	NAD
24	NAD	NAD	NAD	NAD	NAD
25	NAD	NAD	NAD	NAD	NAD
26	NAD	NAD	NAD	NAD	NAD
27	NAD	NAD	NAD	NAD	NAD
28	NAD	NAD	NAD	NAD	NAD
29	NAD	NAD	NAD	NAD	NAD
30	NAD	NAD	NAD	NAD	NAD

APPENDIX B - POSITIVE CONTROL STUDY: CHALLENGE RESPONSES

RESULTS:-

Y07859/001
undiluted
TOP RIGHT

	ANIMAL	SEX	24 HRS	48 HRS
TEST:	1	F	0	0
	2	F	0	0
	3	F	0	0
	4	F	0	0
	5	F	0	0
	6	F	1	0
	7	F	0	0
	8	F	0	0
	9	F	1	0
	10	F	0	0
	11	F	0	0
	12	F	0	0
	13	F	0	0
	14	F	0	0
	15	F	0	0
	16	F	0	0
	17	F	1	0
	18	F	0	0
	19	F	0	0
	20	F	1	0

0 - NO REACTION
1 - SCATTERED MILD REDNESS
2 - MODERATE AND DIFFUSE REDNESS
3 - INTENSE REDNESS AND SWELLING

APPENDIX B - POSITIVE CONTROL STUDY: CHALLENGE RESPONSES

RESULTS:-

			Y07859/001 undiluted TOP RIGHT	
	ANIMAL	SEX	24 HRS	48 HRS
CONTROL:	21	F	0	0
	22	F	0	0
	23	F	0	0
	24	F	0	0
	25	F	0	0
	26	F	0	0
	27	F	0	0
	28	F	0	0
	29	F	0	0
	30	F	0	0

0 - NO REACTION
1 - SCATTERED MILD REDNESS
2 - MODERATE AND DIFFUSE REDNESS
3 - INTENSE REDNESS AND SWELLING

APPENDIX B - POSITIVE CONTROL STUDY: BODYWEIGHTS (g)

DOSE: TEST

ANIMAL NUMBER	DAY -1	DAY 31
FEMALES		
1	386	504
2	388	503
3	402	492
4	391	530
5	406	558
6	393	525
7	378	480
8	389	505
9	412	529
10	384	493
11	355	460
12	409	595
13	414	540
14	437	596
15	368	484
16	397	484
17	408	522
18	378	478
19	404	517
20	393	518

APPENDIX B - POSITIVE CONTROL STUDY: BODYWEIGHTS (g)

DOSE: CONTROL

ANIMAL NUMBER	DAY -1	DAY 31
FEMALES		
21	406	541
22	380	523
23	348	439
24	404	532
25	392	502
26	380	462
27	380	477
28	425	548
29	438	567
30	400	553

APPENDIX C - MAIN STUDY: BODYWEIGHTS (g)

DOSE: TEST

ANIMAL NUMBER	DAY -1	DAY 40
FEMALES		
331	277	425
332	294	479
333	303	496
334	265	412
336	286	447
337	287	479
338	268	469
339	262	454
340	282	430
341	272	496
342	284	468
343	278	457
344	288	416
345	284	458
346	282	446
347	269	480
348	291	504
349	263	481
350	268	431

APPENDIX C - MAIN STUDY: BODYWEIGHTS (g)

DOSE: CONTROL (FIRST CHALLENGE)

ANIMAL NUMBER	DAY -1	DAY 31
FEMALES		
351	282	461
352	277	475
353	300	472
354	294	470
355	267	431
356	296	470
357	280	451
358	281	459
359	275	466
360	255	411

APPENDIX C - MAIN STUDY: BODYWEIGHTS (g)

DOSE: CONTROL (SECOND CHALLENGE)

ANIMAL NUMBER	DAY -1	DAY 3
FEMALES		
423	523	512
424	411	493
425	523	492
426	507	492
427	500	452
428	545	532
429	601	576
430	515	510
431	517	496
432	550	497

CERTIFICATE OF ANALYSIS

syngenta

GLP Testing Facility EZA
Analytical Development &
Product Chemistry GS2131

Syngenta Crop Protection
Münchwilen AG
Breitenloh 5
CH-4333 Münchwilen

Certificate of Analysis

A13735F
CGA15324/lambda-cyhalothrin EC (300/015)
SEZ3CP001

Batch Identification	**SEZ3CP001**
Product Code	**A13735F**
Other Product Code(s)	CGA15324/lambda-cyhalothrin EC (300/015)

Chemical Analysis
(Active Ingredient Content)

– **Identity of the Active Ingredients ***	**confirmed**
– **Content of:**	
- CGA15324 *	**302 g/l**
- lambda-cyhalothrin *	**15.6 g/l**
Methodology used for Characterization	wide-bore GC

The Active Ingredient(s) content is within the FAO limits.

Physical Analysis

– **Appearance**	**Yellow-orange liquid**
– **Density ***	**1103 kg/m^3**

Stability:

– **Storage Temperature**	**< 30°C, keep away from direct sunlight**
– **Reanalysis date**	**July 2005**

The stability of this test substance will be controlled by reanalysis of material held in the inventory at Syngenta Crop Protection Münchwilen AG at the appropriate time.

This Certificate of Analysis is summarizing data which originate either from a single study or from several individual studies which have been performed in compliance with GLP. Tests marked with an asterisk (*) have been conducted within a single study/as individual studies. Raw data, documentation, study plans, any amendments to study plans and reports pertaining to this/these studie(s) are stored under the study number(s) referenced below within the archives of the GLP Testing Facility EZA at Syngenta Crop Protection Münchwilen AG. No GLP compliance is claimed for this certificate.

Characterisation: 110305 Reanalysis:

Authorisation: May 21, 2003

Siegfried Voellmin
Analytical Development & Product Chemistry