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Propiconazole/Fenpropidin

Propiconazole/Fenpropidin EC (A9050B) - The *In Vitro* Percutaneous Absorption of Radiolabelled Propiconazole and Radiolabelled Fenpropidin in Concentrate Formulation and Two In-Use Dilutions Through Human Split-Thickness Skin

Final Report

TEST GUIDELINE(S): OECD 428 (2004)

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COMPLETION DATE: 09 June 2022

PERFORMING LABORATORY: Charles River Laboratories Edinburgh Ltd
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United Kingdom

LABORATORY PROJECT ID: Report Number: 788252
Study Number: 788252
Task Number: TK0546546

SPONSOR(S): Syngenta Ltd
Jealott's Hill International Research Centre
Bracknell, Berkshire, RG42 6EY, United Kingdom

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410 Swing Road
Post Office Box 18300
Greensboro, NC 27419-8300 USA

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Study Number: 788252
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Test Item: Propiconazole/Fenpropidin

I, the undersigned, hereby declare that this study was performed in accordance with the OECD Principles of Good Laboratory Practice as incorporated into the United Kingdom Statutory Instrument for GLP and as accepted by Regulatory Authorities throughout the European Union, United States of America (FDA and EPA), Japan (MHLW, MAFF and METI) and other countries that are signatories to the OECD Mutual Acceptance of Data Agreement.

The study was conducted according to the procedures herein described and this report represents a true and accurate record of the results obtained.

09 Jun 2022

Leigh Dickson, BSc
Study Director

Date

Performing Laboratory:
Charles River Laboratories Edinburgh Ltd
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United Kingdom

To be completed for USA EPA submission only:
Representative of Submitter/Sponsor:

Date

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FLAGGING STATEMENT

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QUALITY ASSURANCE STATEMENT

Study Number: 788252
Sponsors Ref: TK0546546

Study Title: Propiconazole/Fenpropidin EC (A9050B)- The *In Vitro* Percutaneous Absorption of Radiolabelled Propiconazole and Radiolabelled Fenpropidin in Concentrate Formulation and Two In-Use Dilutions Through Human Split-Thickness Skin

Test Item: Propiconazole/Fenpropidin

The Charles River Quality Assurance Unit conducted a protocol review, protocol amendments review(s), process-based inspections and report audits relevant to this short-term study, as detailed below.

QA INSPECTION DATES

		Dates Findings Submitted to:	
Date(s) of Audit	Phase(s) Audited	Study Director	Test Facility Management
09-Nov-2021	Split Thickness Skin Preparation	N/A	09-Nov-2021
10-Nov-2021	Barrier Integrity Test	N/A	10-Nov-2021
10-Nov-2021	Receipt of Skin	N/A	10-Nov-2021
12-Nov-2021	Terminal Procedures	N/A	12-Nov-2021
09-Nov-2021	Radiolabelled Dose Preparation	N/A	09-Nov-2021
01-Nov-2021	Particle Size Analysis	N/A	01-Nov-2021
12-Nov-2021	Sample Preparation for Total Radioactivity and LSC	N/A	12-Nov-2021
08-Nov-2021	Final Protocol	08-Nov-2021	08-Nov-2021
23-Nov-2021	Dose Administration	23-Nov-2021	23-Nov-2021
26-Nov-2021	Protocol Amendment 01	26-Nov-2021	26-Nov-2021
29-Nov-2021	Protocol Amendment 02	29-Nov-2021	29-Nov-2021
01-Dec-2021	Protocol Amendment 03	01-Dec-2021	01-Dec-2021
14-Mar-2022 – 16-Mar-2022	Report	16-Mar-2022	16-Mar-2022
22-Mar-2022	Protocol Amendment 04	22-Mar-2022	22-Mar-2022
03-May-2022	Final Report	03-May-2022	03-May-2022

The protocol review, protocol amendment review(s) and report audits were reported to the Study Director on the same day as reported to Management. The outcome of each process-based inspection is also reported to the Study Director, where relevant.

Facilities relevant to this study are included in Charles River's annual facility inspection programme. The outcome of each inspection is reported to Management.

This report is considered to describe accurately and completely the procedures used in the study and the results obtained.

Lisa Martin
Lisa Martin, BSc
Quality Assurance

09 Jun 2022
Date

GENERAL INFORMATION

Contributors
The following contributed to this report in the capacities indicated:

Name	Title
Leigh Dickson, BSc	Study Director
Larra Cairns	Report Author
Jennifer MacCalman, BSc	Report Author
Jennifer Leak, BSc	Individual Scientist (High Performance Liquid Chromatography (HPLC) Analysis)
Lisa Martin, BSc	QA Auditor
Jeffrey Davis, BS, MBA	Sponsor Representative

Study Dates
Study Initiation Date: 05 November 2021
Experimental Start Date: 15 November 2021
Experimental Completion Date: 14 February 2022

Deviations from the Guidelines
None.

Retention of Samples
All samples will be discarded following completion of the study.

Performing Laboratory Test Substance Reference Number
[^{14}C]-Propiconazole, [PHENYL-U-14C]-CGA064250, Batch No. ATS-21-57212-2, Dispense No. 210C6B
[^{14}C]-Fenpropidin, [N-METHYLPROPYL-3-14C]-CGA114900, Batch No. NP-21-58296-2, Dispense No. 210CB8
Propiconazole, Batch No. WRS 1329/1, Dispense No. 210A76
Fenpropidin Tech., Batch No. UU20017829, Dispense No. 210CA2
A9050B, Batch No. STH001-015-001, Dispense No. 210ABC
EXF25384A, Batch No. GOM001-053-001, Dispense No. 210C01
EXF25385A, Batch No. GOM001-053-002, Dispense No. 210C02

Other
All study-specific raw data, documentation, protocol and protocol amendments from this study were transferred to the Test Facility archive by no later than the date of final report issue unless otherwise specified in the protocol. Five years after issue of the final report, the Sponsor will be contacted to determine the disposition of materials associated with the study.

Electronic data generated by the Test Facility were archived as noted above, except for the reporting files stored on M-Files and notes to file recorded on Deviation Information Library (DevIL), which were archived at the Charles River Laboratories facility located in Wilmington, MA.

A reserve sample of the test item, formulation and blank formulation, with the exception of the radiolabelled test item, will be retained in the Scientific Archive of Charles River Laboratories Edinburgh Ltd under the appropriate storage conditions. The original signed copy of the final report will be stored indefinitely in the Scientific Archives of Charles River Laboratories Edinburgh Ltd.

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1.0 EXECUTIVE SUMMARY

1.1 Study Design

The rate and extent of absorption of [^{14}C]-Propiconazole and [^{14}C]-Fenpropidin following topical application as an emulsifiable concentrate formulation (EC) was measured *in vitro* through human split-thickness skin. The concentration of propiconazole in the formulation concentrate, spray dilution 1 and spray dilution 2 was *ca* 125 g/L, *ca* 6.25 g/L and 0.625 g/L, respectively. The concentration of fenpropidin in the formulation concentrate, spray dilution 1 and spray dilution 2 was *ca* 275 g/L, *ca* 13.75 g/L and 1.375 g/L, respectively.

The doses were applied at 10 µL/cm^2 and left unoccluded (with the exception of [^{14}C]-Fenpropidin in Spray Dilution 1 and [^{14}C]-Fenpropidin in Spray Dilution 2, which were occluded with traps containing carbon filters) for an experimental period of 24 h, with an interim wash at 6 h post-application.

The absorption process was followed by taking samples of the receptor fluid, phosphate buffered saline containing polyoxyethylene 20 oleyl ether (PEG, *ca* 6%, w/v), sodium azide (*ca* 0.01%, w/v), streptomycin (*ca* 0.1 mg/mL) and penicillin (*ca* 100 units/mL), pH 7.4 ± 0.1, at recorded intervals throughout the experimental period.

The distribution of propiconazole and fenpropidin within the test system and a 24 h absorption profile was determined using liquid scintillation counting. Before conducting the main study, stability and solubility assessments were carried out.

1.2 Results

1.2.1 [^{14}C]-Propiconazole in formulation concentrate (125 g/L)

The mean absorption rate of [^{14}C]-Propiconazole from the formulation concentrate through human split-thickness skin was 0.31 µg equiv./cm^2/h during the 24 h experimental period. The amount penetrated at 24 h, as measured in the receptor fluid, was 7.47 µg equiv./cm^2 (0.59% of the applied dose).

Following the skin wash at 6 h, 94.46% of the applied dose of [^{14}C]-Propiconazole was washed off. At 24 h post dose, a further 0.76% was removed during the skin wash. A proportion of the dose applied was recovered from the donor chamber wash (0.12%), exposed skin (0.26%) and receptor chamber wash (0.06%). The mean total recovery was 96.39% of the applied dose.

1.2.2 [^{14}C]-Propiconazole in spray dilution 1 (6.25 g/L)

The mean absorption rate of [^{14}C]-Propiconazole from spray dilution 1 through human split-thickness skin was 0.16 µg equiv./cm^2/h during the 24 h experimental period. The

amount penetrated at 24 h, as measured in the receptor fluid, was 3.92 µg equiv./cm^2 (6.34% of the applied dose).

Following the skin wash at 6 h, 80.78% of the applied dose of [^{14}C]-Propiconazole was washed off. At 24 h post dose, a further 4.18% was removed with the skin wash. A proportion of the dose applied was recovered from the donor chamber wash (0.81%), exposed skin (1.88%) and receptor chamber wash (0.51%). The mean total recovery was 95.08% of the applied dose.

1.2.3 [^{14}C]-Propiconazole in spray dilution 2 (0.625 g/L)

The mean absorption rate of [^{14}C]-Propiconazole from spray dilution 2 through human split-thickness skin was 0.04 µg equiv./cm^2/h during the 24 h experimental period. The amount penetrated at 24 h, as measured in the receptor fluid, was 0.88 µg equiv./cm^2 (13.28% of the applied dose).

Following the skin wash at 6 h, 68.24% of the applied dose of [^{14}C]-Propiconazole was washed off. At 24 h post dose, a further 6.40% was removed with the skin wash. A proportion of the dose applied was recovered from the donor chamber wash (1.10%), exposed skin (3.99%) and receptor chamber wash (0.81%). The mean total recovery was 94.91% of the applied dose.

1.2.4 [^{14}C]-Fenpropidin in formulation concentrate (275 g/L)

The mean absorption rate of [^{14}C]-Fenpropidin from the formulation concentrate through human split-thickness skin was 1.17 µg equiv./cm^2/h during the 24 h experimental period. The amount penetrated at 24 h, as measured in the receptor fluid, was 28.2 µg equiv./cm^2 (1.02% of the applied dose).

Following the skin wash at 6 h, 92.55% of the applied dose of [^{14}C]-Fenpropidin was washed off. At 24 h post dose, a further 1.16% was removed during the skin wash. A proportion of the dose applied was recovered from the donor chamber wash (0.19%), exposed skin (0.47%) and receptor chamber wash (0.08%). The mean total recovery was 95.74% of the applied dose.

1.2.5 [^{14}C]-Fenpropidin in spray dilution 1 (13.75 g/L)

The mean absorption rate of [^{14}C]-Fenpropidin from spray dilution 1 through human split-thickness skin was 0.42 µg equiv./cm^2/h during the 24 h experimental period. The amount penetrated at 24 h, as measured in the receptor fluid, was 10.1 µg equiv./cm^2 (6.83% of the applied dose).

Following the skin wash at 6 h, 79.88% of the applied dose of [^{14}C]-Fenpropidin was washed off. A proportion of the dose applied was recovered from the 6 h filter (0.32%). At 24 h post dose, a further 3.07% was removed with the skin wash. A proportion of the dose applied was

recovered from the donor chamber wash/trap (0.52%), 24 h filter (0.27%), exposed skin (2.48%) and receptor chamber wash (0.44%). The mean total recovery was 95.13% of the applied dose.

1.2.6 [^{14}C]-Fenpropidin in spray dilution 2 (1.375 g/L)

The mean absorption rate of [^{14}C]-Fenpropidin from spray dilution 2 through human split-thickness skin was 0.07 µg equiv./cm^2/h during the 24 h experimental period. The amount penetrated at 24 h, as measured in the receptor fluid, was 1.59 µg equiv./cm^2 (11.10% of the applied dose).

Following the skin wash at 6 h, 71.21% of the applied dose of [^{14}C]-Fenpropidin was washed off. A proportion of the dose applied was recovered from the 6 h filter (1.37%). At 24 h post dose, a further 4.66% was removed with the skin wash. A proportion of the dose applied was recovered from the donor chamber wash/trap (1.13%), 24 h filter (0.70%), exposed skin (2.81%) and receptor chamber wash (0.67%). The mean total recovery was 95.04% of the applied dose

1.3 Conclusion

The study demonstrated that the amount of propiconazole absorbed through human split-thickness skin membranes over 24 h (following a 6 h exposure) from the formulation concentrate (125 g/L) and the intended in-use dilutions (6.25 g/L and 0.625 g/L) was 0.64%, 6.85%, and 14.09% of the applied dose, respectively, as measured in the receptor fluid and receptor chamber wash. The amount of fenpropidin absorbed through human split-thickness skin membranes over 24 h (following a 6 h exposure) from the formulation concentrate (275 g/L) and the intended in-use dilutions (13.75 g/L and 1.375 g/L) was 1.10%, 7.28%, and 11.77% of the applied dose, respectively, as measured in the receptor fluid and receptor chamber wash.

2.0 INTRODUCTION

2.1 Purpose

The purpose of this study was to determine the rate and extent of the *in vitro* percutaneous absorption of propiconazole and fenpropidin through human split-thickness skin (following 6 h exposure) over an experimental period of 24 h to aid the quantitative assessment of the risk arising from skin contact with propiconazole and fenpropidin in an emulsifiable concentrate (EC) formulation concentrate and two in-use spray dilutions.

The active ingredient (propiconazole) was assessed with the following applications:

- Formulation concentrate (125 g/L)
- Spray dilution 1 (6.25 g/L)
- Spray dilution 2 (0.625 g/L)

The active ingredient (fenpropidin) was assessed with the following applications:

- Formulation concentrate (275 g/L)
- Spray dilution 1 (13.75 g/L)
- Spray dilution 2 (1.375 g/L)

2.2 Regulatory Guidelines and Guidance Documents

This study was conducted according to Charles River Protocol No. 788252 and Protocol Amendment No. 3. This study was performed in accordance with Good Laboratory Practice regulations. A copy of the GLP certificate for Charles River is provided in Appendix 1. This study was conducted in accordance with the following documents.

- OECD Guideline for Testing of Chemicals, Guideline 428: Skin Absorption: *In Vitro* Method (2004).
- OECD Environmental Health and Safety Publications Series on Testing and Assessment No. 28. Guidance Document for the Conduct of Skin Absorption Studies (2004).
- European Commission Guidance Document on Dermal Absorption – Sanco/222/2000/Rev. 7 (19 March 2004).
- Guidance on Dermal Absorption (EFSA Journal, 2017, 15(6): 4873).

2.3 Justification and Selection of the Test System

Split-thickness skin membranes are an accepted system for determining dermal absorption across human skin *in vitro* and its reliability has been demonstrated at Charles River Laboratories under the following study:

Page, L (2020). Inter Laboratory Comparison of The In Vitro Percutaneous Absorption of Radiolabelled Caffeine Through Human Split-Thickness Skin. Charles River Study No. 997161

2.4 Dose Level Selection

The application rates and exposure conditions used in this study were designed to simulate predicted in-use field concentrations of the formulation and were requested by the Sponsor.

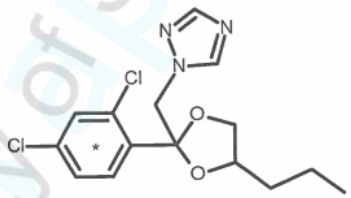
3.0 MATERIALS AND METHODS

3.1 Test and Control Substances

3.1.1 Radiolabelled test item: [^{14}C]-Propiconazole

Name:	[PHENYL-U-^{14}C]-CGA064250
Synonymns:	[PHENYL-U-^{14}C]-CSAA054101
Batch Number:	ATS-21-57212-2
Physical Appearance:	Clear liquid
Radiochemical Purity:	98.9%
Specific Activity:	61.0 µCi/mg
Storage Conditions:	Frozen (-20°C) Refrigerated (+4°C) for *ca* 1 day prior to being moved to -20°C storage.

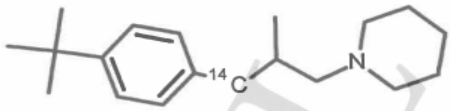
A copy of the Certificate of Analysis is presented in Appendix 2. The structure and site of labelling (*) of [^{14}C]-Propiconazole is shown below.



3.1.2 Radiolabelled test item: [^{14}C]-Fenpropidin

Name:	[N-METHYLPROPYL-3-^{14}C]-CGA114900
Synonymns:	[N-METHYLPROPYL-3-^{14}C]-CSAA104478
Batch Number:	NP-21-58296-2
Physical Appearance:	Yellow liquid
Radiochemical Purity:	99.0%
Specific Activity:	199.5 µCi/mg
Storage Conditions:	Frozen (-20°C)

A copy of the Certificate of Analysis is presented in Appendix 3. The structure and site of labelling (^{14}C) of [^{14}C]-Propiconazole is shown below.



3.1.3 Non-radiolabelled test item: Propiconazole Technical

Name:	Propiconazole
Batch (Lot) Number:	WRS 1329/1
Physical Appearance:	Brownish clear viscous liquid
Purity:	96.3%
Storage Conditions:	Ambient (<30˚C)
Recertification Date:	30 September 2027

The test item is considered stable until the recertification date is reached. An archive sample of non-radiolabelled propiconazole has been retained at Charles River. A copy of the Certificate of Analysis for propiconazole technical is presented in Appendix 4.

3.1.4 Non-radiolabelled test item: Fenpropidin Technical

Name:	Fenpropidin Tech.
Batch (Lot) Number:	UU20017829
Physical Appearance:	Colorless liquid
Purity:	100.4%
Storage Conditions:	Ambient (<30˚C)
Recertification Date:	31 March 2023

The test item is considered stable until the recertification date is reached. An archive sample of non-radiolabelled fenpropidin has been retained at Charles River. A copy of the Certificate of Analysis for fenpropidin technical is presented in Appendix 5.

3.1.5 Commercial formulation

Name:	A9050B
Alternative Name:	Propiconazole/fenpropidin EC (125/275)
Batch Number:	STH001-015-001
Physical Appearance:	Light yellow liquid
Storage Conditions:	Ambient (<30˚C)
Density:	953 kg/m^3
Recertification Date:	30 September 2025

The commercial formulation is considered stable until the recertification date is reached. An archive sample of the commercial formulation has been retained at Charles River. A copy of the Certificate of Analysis is presented in Appendix 6.

3.1.6 Blank formulation

Name:	EXF25384A
Alternative Name:	Blank of A9050B propiconazole
Batch Number:	GOM001-053-001
Storage Conditions:	Ambient (<30˚C)
Expiry Date:	18 October 2023

Name:	EXF25385A
Alternative Name:	Blank of A9050B fenpropidin
Batch Number:	GOM001-053-002
Storage Conditions:	Ambient (<30˚C)
Expiry Date:	18 October 2023

An archive sample of the blank formulations has been retained at Charles River.

3.1.7 Other materials

Sigma-Aldrich Company Limited supplied phosphate buffered saline, penicillin-streptomycin solution, polyoxyethylene 20 oleyl ether (PEG) (commercial name BRIJ®020), sodium azide, trifluoroacetic acid, phosphoric acid and tin (II) chloride dihydrate.
Scientific Laboratory Supplies provided ethanol.
Fisher Scientific water D solution.
Zinsser Analytic supplied Aquasafe 500 plus® liquid scintillation fluid.
Meridian Biotechnologies Limited provided the ProFlow G+ scintillation fluid and Scintanol.
Perkin Elmer provided Solvable™.
VWR Chemicals supplied acetonitrile.
Unilever UK supplied Simple Kind to Skin handwash.

All other materials were obtained by Charles River.

3.2 Confirmation of Concentration of [^{14}C]-Propiconazole Stock Solution

Three aliquots (10 µL) were removed from [^{14}C]-Propiconazole stock solution (Specific Activity (S.A.) 61.0 µCi/mg; Section 3.1.1) into vials and mixed with acetonitrile (10 mL). The contents were shaken to mix. Duplicate aliquots (1 mL) were removed, mixed with scintillation fluid and analysed by liquid scintillation counting.

By radioactivity, the concentration of [^{14}C]-Propiconazole in the stock solution was 4.708 mg/mL. The stock solution was homogeneous with a coefficient of variance (CV) of 0.94%.

3.3 Confirmation of Concentration of [^{14}C]-Fenpropidin Stock Solution

Three aliquots (10 µL) were removed from [^{14}C]-Fenpropidin stock solution (S.A. 199.5 µCi/mg; Section 3.1.2) into vials and mixed with acetronitrile (10 mL). The contents were shaken to mix. Duplicate aliquots (1 mL) were removed, mixed with scintillation fluid and analysed by liquid scintillation counting.

By radioactivity, the concentration of [^{14}C]-Fenpropidin in the stock solution was 2.243 mg/mL. The stock solution was homogeneous with a CV of 2.23%.

3.4 Confirmation of Radiochemical Purity of [^{14}C]-Propiconazole

An aliquot (5 µL) of [^{14}C]-Propiconazole stock solution (S.A. 61.0 µCi/mg; Section 3.1.1) was dissolved in acetronitrile (300 µL). Propiconazole (22.72 mg) was dissolved in acetonitrile (11 mL) and mixed by vortex. A U.V. standard was prepared by removing propiconazole solution (5 mL) into a new vial, acetonitrile (5 mL) was added and mixed by vortex. The U.V. standard (50 µL) was added to the radiochemical solution, mixed by vortex and analysed by high performance liquid chromatography (HPLC). The radiochemical purity of [^{14}C]-Propiconazole was determined using the following equipment and conditions:

Equipment

HPLC Model:	1100 Series
Radio-detector Model:	β-RAM Model 4
Scintillant:	ProFlow G+
Scintillant Flow Rate:	2 mL/min
Column:	Hichrom ACE C18 (250 mm x 4 mm, 5 µm)

Conditions

Solvent A:	Milli-Q Water
Solvent B:	Acetonitrile
Mobile Phase Conditions:	Gradient
Run Time:	35 min
Flow Rate:	1 mL/min
Column Temperature:	40°C
Auto-sampler Temperature:	25°C
U.V. Detector Wavelength:	220 nm

	Time (min)	Solvent A (%)	Solvent B (%)
	0	70	30
	5	70	30
	10	60	40
	15	50	50
	25	0	100
	30	0	100
	30.1	70	30
	35	70	30
Post time	5	70	30

Data was captured by Laura software. The chemical authenticity of the radiolabelled test item was confirmed by co-chromatography with authentic non-radiolabelled test item. The radiochemical purity of [^{14}C]-Propiconazole was determined to be 97.8%. A representative HPLC chromatogram is presented in Appendix 7.

3.5 Confirmation of Radiochemical Purity of [^{14}C]-Fenpropidin

An aliquot (5 µL) of [^{14}C]-Fenpropidin stock solution (S.A. 199.5 µCi/mg; Section 3.1.2) was dissolved in acetonitrile (460 µL). A U.V. standard was prepared by dissolving fenpropidin technical (21.77 mg) in acetonitrile (21 mL). The U.V. standard (160 µL) was added to the radiochemical solution, mixed by vortex and analysed by high performance liquid chromatography (HPLC). The radiochemical purity of [^{14}C]-Fenpropidin was determined using the following equipment and conditions:

Equipment

HPLC Model:	1100 Series
Radio-detector Model:	β-RAM Model 4
Scintillant:	ProFlow G+
Scintillant Flow Rate:	2 mL/min
Column:	Luna C18 (2) (250 mm x 4.6 mm, 5 µm)

Conditions

Solvent A:	0.1% Phosphoric Acid (aq)
Solvent B:	0.1% Phosphoric Acid in Acetonirtile
Mobile Phase Conditions:	Gradient
Run Time:	30 min
Flow Rate:	1 mL/min
Column Temperature:	40°C
Auto-sampler Temperature:	4°C
U.V. Detector Wavelength:	254 nm

	Time (min)	Solvent A (%)	Solvent B (%)
		80	20
	0	80	20
	5	0	100
	20	0	100
	25	80	20
	25.1	80	20
Post Time	5	80	20

Data was captured by Laura software. The chemical authenticity of the radiolabelled test item was confirmed by co-chromatography with authentic non-radiolabelled test item. The radiochemical purity of [^{14}C]-Fenpropidin was determined to be 97.8%. A representative HPLC chromatogram is presented in Appendix 8.

3.6 Human Skin Samples

Twelve samples of full-thickness human skin (abdomen) were obtained from male and female donors aged 34 to 56 years old. Eleven samples were received from Tissue Solutions, Glasgow. One sample was received from Biopredic International. The samples arrived at Charles River deep frozen on dry ice and were stored in a freezer set to maintain a temperature of -20°C until used in the study. The age and sex of the donor and site from which the skin was taken were recorded centrally and in the study records. The details are shown in Appendix 9.

3.7 Preparation of Split-Thickness Skin

All skin samples were removed from storage and allowed to thaw at ambient temperature. The thickness of the uncut skin membranes was measured using a micrometer. Split-thickness membranes were prepared by pinning the full-thickness skin, *stratum corneum* uppermost, onto a raised cork board and cutting at a setting equivalent to 200-400 µm depth using a Zimmer® electric dermatome. The thickness of the membranes was measured using a micrometer. The membranes were then wrapped in aluminium foil and stored in a freezer set to maintain a temperature of -20°C and used within two months. The thickness of the full-thickness and split-thickness skin membranes is provided in Appendix 10.

3.8 Static Diffusion Cell Apparatus

A static diffusion cell system (PermeGear Inc) was used (see the following photograph). The static diffusion cells were placed in a manifold on a magnetic stirrer plate heated *via* a circulating water bath to maintain the skin surface temperature at 32°C ± 1°C. The actual cell temperatures (ranging from 31.1°C to 32.9°C) were calibrated prior to mounting of the skin cells.

The surface area of exposed skin within the cells was 0.64 cm^2. The receptor chamber volume was nominally 5 mL, with each receptor chamber individually marked with the actual volume by the manufacturer.

A Photograph of a Static Diffusion Cell and a Static Diffusion Cell in the Heated Manifold

3.9 Receptor Fluid

The receptor fluid chosen for use in this study was phosphate buffered saline containing polyoxyethylene 20 oleyl ether (PEG, *ca* 6%, w/v), sodium azide (*ca* 0.01%, w/v), streptomycin (0.1 mg/mL) and penicillin (100 units/mL). The pH of the receptor fluid was checked and adjusted (if required) and the pH ranged between 7.32-7.43.

3.10 Solubility of the Test Item in Receptor Fluid

Propiconazole was predicted to have a water solubility of 0.1 g/L at 20ºC (The Pesticide Manual, Sixteenth Edition). For an application of 10 µL/cm^2 over a 0.64 cm^2 application area, for the highest concentration formulation (125 g/L), 6.4 mg of formulation would be applied to each skin sample. A 25% default absorption value can be applied for emulsifiable concentrate formulations, as recommended in EFSA Journal, 2017, 15 (6): 4873. Theoretically, if 25% of propiconazole was absorbed, this would result in a test item concentration in the receptor fluid of 40 mg/L.

Fenpropidin was predicted to have a water solubility of 0.53 g/L (pH 7), 0.0062 g/L (pH9) at 25ºC (The Pesticide Manual, Sixteenth Edition). For an application of 10 µL/cm^2 over a 0.64 cm^2 application area, for the highest concentration formulation (275 g/L), 6.4 mg of formulation would be applied to each skin sample. A 25% default absorption value can be applied for emulsifiable concentrate formulations, as recommended in EFSA Journal, 2017, 15 (6): 4873. Theoretically, if 25% of fenpropidin was absorbed, this would result in a test item concentration in the receptor fluid of 88 mg/L.

Subsequently, the solubility of both test items in the receptor fluid was determined.

3.11 Solubility Assessment

3.11.1 Propiconazole

[^{14}C]-Propiconazole stock solution (10 µL, S.A. 61.0 µCi/mg, Section 3.1.1) was added to a 1 mL volumetric flask. The solvent was removed under a gentle stream of nitrogen gas. Propiconazole (29.94 mg, Section 3.1.3) was added to the flask. Ethanol was added up to the 1 mL calibration line and the contents were vortex mixed until the contents were visually fully dissolved. Three aliquots (10 µL) were taken into vials, mixed with Scintanol and analysed by liquid scintillation counting.

By radioactivity, the concentration of [^{14}C]-Propiconazole was determined to be 28.9 mg/mL taking into account purity. [^{14}C]-Propiconazole was homogeneously distributed within the solution with a CV of 2.00% and the S.A. was determined to be 0.105 µCi/mg.

[^{14}C]-Propiconazole (346 µL, S.A. 0.105 µCi/mg) was transferred into each of two 25 mL volumetric flasks. The flasks were then filled to the calibration line with either receptor fluid or ethanol (positive control). A magnetic stirrer bar was added and the flask contents were incubated in a waterbath at a temperature of *ca* 32°C for *ca* 1 h, while mixing on a magnetic stirring plate. Following incubation, the contents of each flask were transferred into 50 mL Falcon® tubes which were centrifuged at *ca* 2000 *g* for *ca* 5 min. Triplicate aliquots (1 mL) of the resultant supernatant were taken, mixed with scintillation fluid and analysed by liquid scintillation counting.

The results are provided in the following table:

Sample Type	Concentration of Propiconazole in Solution (g/L)	% of Target Propiconazole Concentration	CV (%)
Receptor Fluid	0.323	80.87	0.33
Ethanol	0.420	104.89	0.08

The target concentration (*ca* 0.4 g/L) represented 10 times the default value (25% absorption for an emulsifiable concentrate formulation as defined by EFSA Journal (2017). As 80.87% of the target concentration was accepted into the receptor fluid, the receptor fluid was deemed not to be rate limiting to absorption.

3.11.2 Fenpropidin

[^{14}C]-Fenpropidin stock solution (10 µL, S.A. 199.5 µCi/mg, Section 3.1.2) was added to a 1 mL volumetric flask. The solvent was removed under a gentle stream of nitrogen gas. Fenpropidin tech. (64.11 mg, Section 3.1.4) was added to the flask. Ethanol was added up to the 1 mL calibration line and the contents were vortex mixed until the contents were visually fully dissolved. Three aliquots (10 µL) were taken into vials, mixed with Scintanol and analysed by liquid scintillation counting.

By radioactivity, the concentration of [^{14}C]-Fenpropidin was determined to be 64.1 mg/mL. [^{14}C]-Fenpropidin was homogeneously distributed within the solution with a CV of 0.63% and the S.A. was determined to be 0.0625 µCi/mg.

[^{14}C]-Fenpropidin (343 µL, S.A. 0.0625 µCi/mg) was transferred into each of two 25 mL volumetric flasks. The flasks were then filled to the calibration line with either receptor fluid or ethanol (positive control). A magnetic stirrer bar was added and the flask contents were incubated in a waterbath at a temperature of *ca* 32°C for *ca* 1 h, while mixing on a magnetic stirring plate. Following incubation, the contents of each flask were transferred into 50 mL Falcon® tubes which were centrifuged at *ca* 2000 *g* for *ca* 5 min. Triplicate aliquots (1 mL) of the resultant supernatant were taken, mixed with scintillation fluid and analysed by liquid scintillation counting.

The results are provided in the following table:

Sample Type	Concentration of Fenpropidin in Solution (g/L)	% of Target Fenpropidin Concentration	CV (%)
Receptor Fluid	0.478	54.33	2.46
Ethanol	0.924	105.03	0.23

The target concentration (*ca* 0.88 g/L) represented 10 times the default value (25% absorption for an emulsifiable concentrate formulation as defined by EFSA Journal (2017). As 54.33% of the target concentration was accepted into the receptor fluid, the receptor fluid was deemed not to be rate limiting to absorption.

3.12 Formulation of Test Preparations for Stability Assessment

3.12.1 [^{14}C]-Propiconazole in test preparations

A summary of the initial ingredients of [^{14}C]-Propiconazole in the formulation concentrate, spray dilution 1 and spray dilution 2 is provided in the following table. Full details of preparations are retained within the study files.

	[^{14}C]-Propiconazole		
	Formulation Concentrate	Spray Dilution 1	Spray Dilution 2
Volume of [^{14}C]-Propiconazole (µL, 61.0 µCi/mg; Section 3.1.1)	544	1328	N/A
Volume of A9050B Commercial formulation (µL, Section 3.1.5)	1000	N/A	N/A
Mass of EXF25384A Blank formulation (mg, Section 3.1.6)	N/A	41.41	N/A
Volume of Spray Dilution 1 (µL, Section 3.12.3)	N/A	N/A	76
Volume of Water D Solution (µL)	N/A	950	800

N/A = Not Applicable

3.12.2 Preparation of [^{14}C]-Propiconazole in the formulation concentrate

[^{14}C]-Propiconazole (544 µL, S.A. 61.0 µCi/mg; Section 3.1.1) was added to a Fast Prep® tube and the solvent was removed under a gentle stream of nitrogen gas. A9050B (1000 µL; Section 3.1.5) was added to the tube along with a magnetic stirrer bar, and the contents were mixed by vortex and magnetic stirring. Four aliquots (6.4 µL) were collected, mixed with Scintanol, and analysed by liquid scintillation counting. See Section 3.12.5 for results.

3.12.3 Preparation of [^{14}C]-Propiconazole in spray dilution 1

[^{14}C]-Propiconazole (1328 µL; S.A. 61.0 µCi/mg; Section 3.1.1) was added to a Fast Prep® tube and the solvent was removed under a gentle stream of nitrogen gas. EXF25384A blank formulation (41.41 mg; Section 3.1.6) was added to the tube along with a magnetic stirrer bar, and the contents were mixed by vortex and magnetic stirring. Water D solution (750 µL) was added in small aliquots and the tube contents were mixed by vortex and magnetic stirring between each aliquot addition. Four aliquots (6.4 µL) were collected, mixed with ethanol (10 mL) and shaken to mix. Duplicate aliquots (1 mL) were removed, mixed with scintillation fluid and analysed by liquid scintillation counting. An aliquot of [^{14}C]-Propiconazole in spray dilution 1 (76 µL) was removed from the tube for the preparation of [^{14}C]-Propiconazole in spray dilution 2. Due to high concentration, Water D solution (200 µL) was added to [^{14}C]-Propiconazole in spray dilution 1 and the contents mixed by vortex and magnetic stirring. Four aliquots (6.4 µL) were collected, mixed with ethanol (10 mL) and shaken to mix. Duplicate aliquots (1 mL) were removed, mixed with scintillation fluid and analysed by liquid scintillation counting. See Section 3.12.5 for results.

3.12.4 Preparation of [^{14}C]-Propiconazole in spray dilution 2

[^{14}C]-Propiconazole in spray dilution 1 (76 µL, Section 3.12.3) was added to a Fast Prep® tube along with a magnetic stirrer bar. Water D solution (800 µL) was added to the tube, and the contents were mixed by vortex and magnetic stirring. Four aliquots (6.4 µL) were collected, mixed with Scintanol and analysed by liquid scintillation counting. See table in Section 3.12.5 for results.

3.12.5 Results of analysis of [^{14}C]-Propiconazole in formulation concentrate, spray dilution 1 and spray dilution 2

The results of the analysis are summarised in the following table.

Test Preparation	Formulation Concentrate	Spray Dilution 1	Spray Dilution 2
Specific activity of [^{14}C]-Propiconazole (µCi/mg)	61.0	61.0	61.0
Concentration of propiconazole in test preparation by radioactivity (g/L)	127	6.52	0.568
Target concentration of propiconazole in test preparation (g/L)	125	6.25	0.625
Percentage of target (%)	101.87	104.39	90.90
CV (%)	0.87	0.52	0.36

3.12.6 [^{14}C]-Fenpropidin in test preparations

A summary of the initial ingredients of [^{14}C]-Fenpropidin in the formulation concentrate, spray dilution 1 and spray dilution 2 is provided in the following table. Full details of preparations are retained within the study files.

	[^{14}C]-Fenpropidin		
	Formulation Concentrate	Spray Dilution 1	Spray Dilution 2
Volume of [^{14}C]-Fenpropidin (µL, 199.5 µCi/mg; Section 3.1.2)	357	N/A	N/A
Volume of A9050B Commercial formulation (µL, Section 3.1.5)	1000	N/A	N/A
Mass of EXF25385A Blank formulation (mg, Section 3.1.6)	N/A	47.6	N/A
Volume of [^{14}C]-Fenpropidin Radiodilution (µL, Section 3.12.8)	N/A	336	N/A
Volume of Concentrated Spray Dilution 2 (µL, Section 3.12.9)	N/A	N/A	221
Volume of Water D Solution (µL)	N/A	800	750

N/A = Not Applicable

3.12.7 Preparation of [^{14}C]-Fenpropidin in the formulation concentrate

[^{14}C]-Fenpropidin (357 µL, S.A. 199.5 µCi/mg; Section 3.1.2) was added into a glass vial and the solvent was removed under a gentle stream of nitrogen gas. A9050B (1000 µL; Section 3.1.5) was added to the vial along with a magnetic stirrer bar, and the contents were mixed by vortex and magnetic stirring. Six aliquots (6.4 µL) were collected, mixed with Scintanol, and analysed by liquid scintillation counting. See Section 3.12.10 for results.

3.12.8 Preparation of [^{14}C]-Fenpropidin in spray dilution 1

[^{14}C]-Fenpropidin (1016 µL, S.A. 199.5 µCi/mg; Section 3.1.2) was added into a 1 mL volumetric flask and the solvent was removed under a gentle stream of nitrogen gas. Fenpropidin tech. (38.63 mg; Section 3.1.4) was then added to the volumetric flask. The flask was then filled to the calibration line with ethanol and the contents were mixed by vortex until fully dissolved. Three aliquots (10 µL) were removed into vials and mixed with ethanol (10 mL). Duplicate aliquots (1 mL) were removed, mixed with scintillation fluid, and analysed by liquid scintillation counting.

By radioactivity, the concentration of [^{14}C]-Fenpropidin was determined to be 41.0 mg/mL. [^{14}C]-Fenpropidin was distributed within the solution with a CV of 1.11% and the S.A. was determined to be 11.3 µCi/mg.

[^{14}C]-Fenpropidin radiodilution (336 µL; S.A. 11.3 µCi/mg; Section 3.12.8) was transferred into a glass vial. The solvent was removed under a gentle stream of nitrogen gas. EXF25385A blank formulation (47.60 mg; Section 3.1.6) was added to the vial along with a magnetic stirrer bar, and the contents were mixed by vortex and magnetic stirring. Water D

solution (800 µL) was added in small aliquots and the tube contents were mixed by vortex and magnetic stirring between each aliquot addition. Six aliquots (6.4 µL) were collected, mixed with Scintanol and analysed by liquid scintillation counting. See table in Section 3.12.10 for results.

3.12.9 Preparation of [^{14}C]-Fenpropidin in spray dilution 2

[^{14}C]-Fenpropidin in spray dilution 1 (98 µL; Section 3.12.8) was transferred into a small glass vial and set to the side. An initially concentrated spray dilution 2 was prepared by adding Water D solution (850 µL) to the original vial containing [^{14}C]-Fenpropidin in spray dilution 1, the contents was mixed by vortex and magnetic stirring.

Concentrated [^{14}C]-Fenpropidin in spray dilution 2 (221 µL, Section 3.12.8) was added to a small glass vial along with a magnetic stirrer bar. Water D solution (750 µL) was added, and the contents was mixed by vortex and magnetic stirring. Six aliquots (6.4 µL) were collected, mixed with Scintanol and analysed by liquid scintillation counting. See table in Section 3.12.10 for results.

3.12.10 Results of analysis of [^{14}C]-Fenpropidin in formulation concentrate, spray dilution 1 and spray dilution 2

The results of the analysis are summarised in the following table.

Test Preparation	Formulation Concentrate	Spray Dilution 1	Spray Dilution 2
Specific activity of [^{14}C]-Fenpropidin (µCi/mg)	199.5	11.3	11.3
Concentration of fenpropidin in test preparation by radioactivity (g/L)	275	14.1	1.40
Target concentration of fenpropidin in test preparation (g/L)	275	13.75	1.375
Percentage of target (%)	99.90	102.30	101.91
CV (%)	0.63	2.47	0.33

3.13 Stability Assessment

3.13.1 Propiconazole

Following preparation, an aliquot from each of the [^{14}C]-Propiconazole test preparations was diluted with acetonitrile and the radiochemical purity determined using the HPLC method detailed in Section 3.4.

The results of the stability analysis are presented in the following table.

Sample Description	Radiochemical Purity (%)
[^{14}C]-Propiconazole in Formulation Concentrate (0 h)	98.6
[^{14}C]-Propiconazole in Formulation Concentrate (24 h)	98.4
[^{14}C]-Propiconazole in Spray Dilution 1 (0 h)	98.8
[^{14}C]-Propiconazole in Spray Dilution 1 (24 h)	99.0
[^{14}C]-Propiconazole in Spray Dilution 2 (0 h)	99.3
[^{14}C]-Propiconazole in Spray Dilution 2 (24 h)	98.8

Four aliquots of each test preparation were collected at the time of the 0 h and 24 h stability assessment, mixed with Scintanol and analysed by liquid scintillation counting, with the exception of [^{14}C]-Propiconazole in spray dilution 1 aliquots which were mixed with ethanol (10 mL) and duplicate aliquots (1 mL) were removed mixed with scintillation fluid and analysed by liquid scintillation counting. The results of this analysis are provided in the following table.

Test Preparation	Target Propiconazole Concentration (g/L)	Propiconazole Concentration			
		0 h		24 h	
		Mean (g/L)	CV (%)	Mean (g/L)	CV (%)
[^{14}C]-Propiconazole in Formulation Concentrate	125	127	0.87	127	1.42
[^{14}C]-Propiconazole in Spray Dilution 1	6.25	6.52	0.52	6.57	0.52
[^{14}C]-Propiconazole in Spray Dilution 2	0.625	0.568	0.36	0.487	1.32

3.13.2 Fenpropidin

Following preparation, an aliquot from each of the [^{14}C]-Fenpropidin test preparations was diluted with acetonitrile and the radiochemical purity determined using the HPLC method detailed in Section 3.5.

The results of the stability analysis are presented in the following table.

Sample Description	Radiochemical Purity (%)
[^{14}C]-Fenpropidin in Formulation Concentrate (0 h)	98.5
[^{14}C]-Fenpropidin in Formulation Concentrate (24 h)	98.4
[^{14}C]-Fenpropidin in Spray Dilution 1 (0 h)	98.6
[^{14}C]-Fenpropidin in Spray Dilution 1 (24 h)	98.6
[^{14}C]-Fenpropidin in Spray Dilution 2 (0 h)	98.7
[^{14}C]-Fenpropidin in Spray Dilution 2 (24 h)	98.9

Four aliquots of each test preparation were collected at the time of the 0 h and 24 h stability assessment, mixed with Scintanol and analysed by liquid scintillation counting. The results of this analysis are provided in the following table.

Test Preparation	Target Fenpropidin Concentration (g/L)	Fenpropidin Concentration			
		0 h		24 h	
		Mean (g/L)	CV (%)	Mean (g/L)	CV (%)
[^{14}C]-Fenpropidin in Formulation Concentrate	275	275	0.63	275	0.30
[^{14}C]-Fenpropidin in Spray Dilution 1	13.75	14.1	2.47	15.0	0.40
[^{14}C]-Fenpropidin in Spray Dilution 2	1.375	1.40	0.33	1.42	0.83

3.14 Static Diffusion Cell Preparation

The receptor chambers were placed in a manifold and connected to a circulating waterbath. Magnetic stirrer bars were placed in the receptor fluid chambers which were filled with receptor fluid (Section 3.9). Split-thickness skin samples were removed from -20°C storage and allowed to thaw at ambient temperature. Sections of split-thickness human skin (*ca* 1.5 x 1.5 cm) were cut and mounted in the diffusion cells between the donor and receptor chambers. The donor chamber was tightened into place with a clamp. Cells were visually checked to ensure no air bubbles were present in the receptor fluid chamber. Cells were left to equilibrate for a minimum of 5 min, after which there were checked to ensure no cells were leaking.

3.15 Barrier Integrity Assessment

Phosphate buffered saline (1 mL) was then added to the donor chamber and the skin samples were allowed to equilibrate for a minimum of 30 min. The electrical resistance was then measured using a Tinsley Databridge (Model: 6401) set at low voltage alternating current, 1000 Hz with a maximum voltage of 300 mV root-mean-squared in the parallel equivalent circuit mode. Any skin sample exhibiting a resistance less than 7.7 kΩ was excluded from subsequent absorption measurements. A cross reference of skin cell number, donor number and electrical resistance (kΩ) is presented in Appendix 11. The phosphate buffered saline was removed from the skin surface and then the skin was rinsed with water and dried with tissue paper.

3.16 Pre-dose Receptor Fluid Collection

Prior to dosing, a 300 µL (6 x 50 µL aliquots) sample of receptor fluid was collected for analysis by liquid scintillation counting. The receptor fluid volume was then maintained by the addition of fresh receptor fluid up to the calibration line on the receptor chamber collection arm and sealed with Parafilm® to prevent evaporation of receptor fluid. Scintanol was added to all samples followed by analysis by liquid scintillation counting.

3.17 Formulation of Test Preparations

3.17.1 [^{14}C]-Propiconazole in test preparations

The [^{14}C]-Propiconazole in formulation concentrate, spray dilution 1 and spray dilution 2 were prepared in a similar manner to that described in Section 3.12. The formulation concentrate and spray dilution 1 was prepared one day before dosing. Spray dilution 2 was prepared on the day of dosing. Full details are retained in the study files. A summary of the preparation of [^{14}C]-Propiconazole in formulation concentrate, spray dilution 1 and spray dilution 2 is provided in the following table.

	[^{14}C]-Propiconazole		
	Formulation Concentrate	Spray Dilution 1	Spray Dilution 2
Volume of [^{14}C]-Propiconazole (µL, 61.0 µCi/mg; Section 3.1.1)	544	1328	N/A
Volume of A9050B Commercial Formulation (µL, Section 3.1.5)	1000	N/A	N/A
Mass of EXF25384A Blank formulation (mg, Section 3.1.6)	N/A	41.74	N/A
Volume of Spray Dilution 1 (µL, Section 3.12.3)	N/A	N/A	95
Volume of Water D Solution (µL)	N/A	950	800
Concentration of [^{14}C]-Propiconazole by radioactivity (g/L)	127	6.55	0.672
Target concentration of [^{14}C]-Propiconazole (g/L)	125	6.25	0.625
Percentage of target (%)	101.92	104.81	107.54
CV (%)	0.93	0.24	0.53

N/A = Not Applicable

The formulation concentrate and spray dilution 1 were dosed on a second occasion. This is because of the number of cells, dosed with the original test preparations was rejected due to low mass balance subsequently, resulting in a reduced number of cells required to complete the study. The above test preparations were used, therefore the concentration was checked prior to dosing. A summary of the results of the analysis of [^{14}C]-Propiconazole in formulation concentrate and spray dilution 1 dosed on the second occasion is provided in the following table.

	[^{14}C]-Propiconazole	
	Formulation Concentrate	Spray Dilution 1
Concentration of [^{14}C]-Propiconazole by radioactivity (g/L)	128	6.29
Target concentration of [^{14}C]-Propiconazole (g/L)	125	6.25
Percentage of target (%)	102.05	100.59
CV (%)	1.06	0.28

3.17.2 [^{14}C]-Fenpropidin in test preparations

With the exception of spray dilution 2 (Section 3.17.3), [^{14}C]-Fenpropidin test preparations were prepared in a similar manner to that described in Section 3.12. The formulation concentrate and spray dilutions were all prepared one day before the day of dosing. Full details are retained in the study files. A summary of the preparation of [^{14}C]-Fenpropidin in formulation concentrate, spray dilution 1 and spray dilution 2 is provided in the following table.

	[^{14}C]-Fenpropidin		
	Formulation Concentrate	Spray Dilution 1	Spray Dilution 2
Volume of [^{14}C]-Fenpropidin (µL, 199.5 µCi/mg; Section 3.1.2)	357	N/A	N/A
Volume of A9050B Commercial formulation (µL, Section 3.1.5)	1000	N/A	N/A
Mass of EXF25385A Blank formulation (mg, Section 3.1.6)	N/A	47.49	N/A
Volume of [^{14}C]-Fenpropidin Radiodilution (µL, Section 3.12.8)	N/A	336	N/A
Volume of Spray Dilution 1 (µL, Section 3.12.8)	N/A	N/A	93
Volume of Water D Solution (µL)	N/A	900	850
Concentration of [^{14}C]-Fenpropidin by radioactivity (g/L)	275	14.8	1.44
Target concentration of [^{14}C]-Fenpropidin (g/L)	275	13.75	1.375
Percentage of target (%)	99.96	107.54	104.48
CV (%)	1.42	0.49	0.96

N/A = Not Applicable

The formulation concentrate was dosed on a second occasion. This is because of the number of cells, dosed with the original test preparations was rejected due to low mass balance subsequently, resulting in a reduced number of cells required to complete the study. The above test preparations were used, therefore the concentration was checked prior to dosing. A summary of the results of the analysis of [^{14}C]-Fenpropidin in formulation concentrate dosed on the second occasion is provided in the following table.

	[^{14}C]-Fenpropidin
	Formulation Concentrate
Concentration of [^{14}C]-Fenpropidin by radioactivity (g/L)	275
Target concentration of [^{14}C]-Fenpropidin (g/L)	275
Percentage of target (%)	99.95
CV (%)	0.73

3.17.3 [^{14}C]-Fenpropidin in spray dilution 2

[^{14}C]-Fenpropidin in spray dilution 1 (93 µL; Section 3.17.2) was transferred into a small glass vial along with a magnetic stirrer bar. Water D solution (850 µL) was added and the

contents mixed by vortex and magnetic stirring. Four aliquots (6.4 µL) were collected, mixed with Scintanol and analysed by liquid scintillation counting.

3.18 Application of Test Preparations to Human Skin

The [^{14}C]-Propiconazole in formulation concentrate was applied evenly over the surface of the exposed skin of 8 split-thickness samples using a positive displacement pipette set to deliver 6.4 µL (10 µL/cm^2). The donor chambers of the cells were not occluded. Seven representative aliquots of the test preparation were dispensed into vials at the time of dosing, mixed with Scintanol and analysed by liquid scintillation counting. [^{14}C]-Propiconazole in spray dilution 1, [^{14}C]-Propiconazole in spray dilution 2 and all three [^{14}C]-Fenpropidin test preparations were processed as described above for [^{14}C]-Propiconazole in formulation concentrate with the exception that the donor chambers of the cells for [^{14}C]-Fenpropidin test in spray dilution 1 and spray dilution 2 were occluded with traps containing carbon filters. The results of the representative aliquots are provided in the following tables.

On the second dosing occasion, [^{14}C]-Propiconazole in formulation concentrate and spray dilution 1 and [^{14}C]-Fenpropidin in formulation concentrate were processed as described above for [^{14}C]-Propiconazole in formulation concentrate. The results of the representative aliquots are provided in the following tables.

Test Preparation	Target Propiconazole Concentration (g/L)	Propiconazole Concentration			
		Occasion 1		Occasion 2	
		Mean (g/L)	CV (%)	Mean (g/L)	CV (%)
[^{14}C]-Propiconazole in Formulation Concentrate	125	127	0.75	128	1.92
[^{14}C]-Propiconazole in Spray Dilution 1	6.25	6.50	1.69	5.94	4.92
[^{14}C]-Propiconazole in Spray Dilution 2	0.625	0.664	2.57	N/A	N/A

Test Preparation	Target Fenpropidin Concentration (g/L)	Fenpropidin Concentration			
		Occasion 1		Occasion 2	
		Mean (g/L)	CV (%)	Mean (g/L)	CV (%)
[^{14}C]-Fenpropidin in Formulation Concentrate	275	275	1.13	275	3.62
[^{14}C]-Fenpropidin in Spray Dilution 1	13.75	14.7	0.71	N/A	N/A
[^{14}C]-Fenpropidin in Spray Dilution 2	1.375	1.44	0.89	N/A	N/A

Prior to the second dosing occasion of [^{14}C]-Propiconazole in formulation concentrate and spray dilution 1, and [^{14}C]-Fenpropidin in formulation concentrate, the concentration and purity of the test preparations were assessed to ensure they were suitable. The results of this analysis are provided in the following tables.

Test Preparation	Formulation Concentrate	Spray Dilution 1
Specific activity of [^{14}C]-Propiconazole (µCi/mg)	61.0	61.0
Concentration of propiconazole in test preparation by radioactivity (g/L)	128	6.47
Target concentration of propiconazole in test preparation (g/L)	125	6.25
Percentage of target (%)	102.02	103.48
CV (%)	0.57	0.50

Test Preparation	Formulation Concentrate
Specific activity of [^{14}C]-Fenpropidin (µCi/mg)	199.5
Concentration of fenpropidin in test preparation by radioactivity (g/L)	275
Target concentration of fenpropidin in test preparation (g/L)	275
Percentage of target (%)	99.95
CV (%)	0.55

Sample Description	Radiochemical Purity (%)
[^{14}C]-Propiconazole in Formulation Concentrate	98.0
[^{14}C]-Propiconazole in Spray Dilution 1	96.4
[^{14}C]-Fenpropidin in Formulation Concentrate	98.5

3.19 Test Item Stability Confirmation

Immediately after dosing, an aliquot was removed from each of the test preparations and processed and analysed in a similar manner to that described in Section 3.13. The results of this analysis are provided in the table below.

Sample Description	Radiochemical Purity (%)	
	Occasion 1	Occasion 2
Post dose [^{14}C]-Propiconazole in Formulation Concentrate	98.8	98.2
Post dose [^{14}C]-Propiconazole in Spray Dilution 1	98.5	98.6
Post dose [^{14}C]-Propiconazole in Spray Dilution 2	97.9	N/A

Sample Description	Radiochemical Purity (%)	
	Occasion 1	Occasion 2
Post dose [^{14}C]-Fenpropidin in Formulation Concentrate	98.9	97.8
Post dose [^{14}C]-Fenpropidin in Spray Dilution 1	98.6	N/A
Post dose [^{14}C]-Fenpropidin in Spray Dilution 2	98.8	N/A

The results of the radiochemical purity assessment confirmed that the test item was stable over the dosing period in all 6 test preparations.

3.20 Receptor Fluid Sampling

Receptor fluid aliquots were collected at 2, 4, 6, 8 and 12 h post dose as described in Section 3.16. All receptor fluid samples were mixed with Scintanol and analysed by liquid scintillation counting.

3.21 Terminal Exposure (6 h Post Dose)

The exposure period was terminated at 6 h post dose. The carbon filters were removed from the occlusive traps from cells for the [^{14}C]-Fenpropidin test in spray dilution 1 and spray dilution 2. Commercial hand wash soap (*ca* 50 µL) was applied to the skin and the soap gently rubbed on the skin with a tissue swab. The skin was then rinsed with *ca* 5 mL of a *ca* 2% (v/v) commercial soap solution. The soap solution was applied in aliquots (0.5 mL) and each aliquot was aspirated three times with a pipette. The skin was dried with a tissue swab. The process was repeated, and the skin was dried with an additional tissue swab. Once the process was completed, fresh carbon filters were added, and the traps were re-sealed and replaced on the cells.

The carbon filters were pooled in a single 20 mL scintillation vial containing 15 mL ethanol for each cell. These were sonicated for *ca* 10 min and mixed by vortex for *ca* 30 sec. The extracted ethanol samples were transferred into a pre-weighed pot. The process was repeated three times after which the 15 mL ethanol was left in the original 20 mL scintillation vial containing the carbon filter following final extraction.

The soap solution (skin wash) was pooled into a single vial for each cell. This bulk sample was split, the samples mixed with scintillation fluid and analysed by liquid scintillation counting. The tissue swabs were retained separately for analysis to investigate the efficacy of the wash procedure. The pipette tip was cut in half and retained. Scintanol was added to the tissue swabs and pipette tips and samples analysed by liquid scintillation counting. The tissue swab samples were sonicated for *ca* 10 min prior to analysis.

3.22 Terminal Exposure (24 h Post Dose)

After an 18 h monitoring period, *i.e.* at 24 h post dose, the carbon filters were processed as described in Section 3.21. The skin was washed, dried and samples analysed (with the exception of tissue swabs which were pooled into a single vial for each cell) as described in Section 3.21. For propiconaole test preparations, the donor chambers were transferred to a pot containing ethanol (15 mL). Equipment was extracted in ethanol for >30 min, before sonication for *ca* 10 min. The equipment was removed from each pot, solvent samples were split into a total of five vials and mixed with scintillation fluid. For fenpropidin test preparations, the donor chambers (with traps for spray dilution 1 and spray dilution 2) were transferred to a pre-weighed pot containing ethanol (40 mL). Equipment was extracted in the solvent for >30 min, before sonication for *ca* 10 min. The equipment was removed from each pot. Duplicate weighed aliquots (*ca* 1 mL) were collected and mixed with scintillation fluid. The skin was removed from each cell and placed on a piece of tissue to remove any remaining receptor fluid from the underside of the skin. This tissue was placed into the receptor chamber wash vial for that particular cell.

The *stratum corneum* was removed with 20 successive tape strips using D-squame® disks. The skin sample was rotated 90° after each tape strip. If any epidermis was removed or if the epidermis/dermis junction became fragile, the rotation of the skin between each tape strip

was stopped. Each tape strip was placed into an individual vial containing Scintanol and then analysed by liquid scintillation counting. Where epidermis was removed, this is detailed in Appendix 12. The skin under the cell flange (unexposed skin) was cut away from the exposed skin. The exposed and unexposed skin samples were placed into separate vials containing Solvable™ (2 mL). The skin samples were placed into a waterbath set to *ca* 60°C to aid solubilisation. Stannous chloride solution (0.2 g/mL in ethanol; 500 µL) and scintillation fluid were added to each skin sample.

The bulk receptor fluid was removed from each receptor chamber and retained in a vial. The samples were split and mixed with scintillation fluid.

The receptor chambers were rinsed with ethanol (*ca* 20 mL). The solvent was pooled as a single sample. Receptor wash samples were then split into aliquots and mixed with scintillation fluid.

All samples were analysed by liquid scintillation counting.

3.23 Storage of Samples

All samples were stored at ambient temperature prior to analysis.

3.24 Quantification of Total Radioactivity

All samples were counted together with representative blanks using a liquid scintillation analyser (Packard 2100-TR) with automatic quench correction by external standard. Where scintillation fluid was added to the samples, this was 10 mL. Where Scintanol was added, this was 12 mL.

Representative blank sample values were subtracted from sample count rates to give net d.p.m. per sample. Prior to analysis, samples were allowed to stabilise with regard to light and temperature. Preliminary samples to investigate concentration and homogeneity in the dosing formulations were counted for 1 min and reported.

3.25 Limit of Reliable Measurement

A limit of reliable measurement of 30 d.p.m. above background has been instituted in these laboratories. Counts that are below 30 d.p.m. above background represent a true value. This means that data are recorded with values that are less than the limit of reliable measurement. Results calculated from data less than 30 d.p.m. above background have been highlighted with an asterisk (*) in the results tables. The instrumental equipment used to quantify radioactivity records data to a fraction of a d.p.m. and reports these values as a mean rounded value over the counting period (5 min). Tables detailing the limit of reliable measurement for each matrix in each test preparation are provided in Appendix 13.

3.26 Electronic Data Acquisitions and Systems

Total radioactivity and sample weight data was acquired using DEBRA® (version 5.7.10.129) Laboratory Information System (LabLogic Systems Limited).

The data was transferred into Microsoft® Office Excel® for calculation of result tables and graphs.

Chromatography data was acquired using Laura® version 6.1.5.69 (LabLogic Systems Limited).

Deviations and Notes to File were recorded into the Deviation Information Library (DevIL) version 2.2.

M-Files (version 21) was used for reporting and collection of 21 CFR part 11 compliant signatures.

3.27 Calculations

The following calculations were performed:

$$\text{Sample amount (µg equiv./cm}^2\text{)} = \frac{\text{sample radioactivity (d.p.m.)}}{\text{specific activity (d.p.m./µg equiv.) x exposure area (cm}^2\text{)}}$$

$$\text{Sample applied dose (\%)} = \frac{\text{sample radioactivity (d.p.m.)}}{\text{applied dose (d.p.m.)}} \times 100\%$$

3.28 Data Presentation

Data presented in results, tables, figures and appendices are computer generated and rounded appropriately for inclusion in the report. As a consequence, calculation of values from data presented will, in some instances, yield minor variations.

3.29 Definitions

The definitions are taken directly from the OECD Guidance Document No. 28 and are provided in Appendix 14.

3.30 Protocol Deviation

The study was performed in accordance with the protocol and protocol amendments for Charles River Study No. 788252 with no deviations.

4.0 RESULTS AND DISCUSSION

4.1 [^{14}C]-Propiconazole in the Formulation Concentrate, Spray Dilution 1 and Spray Dilution 2

A summary of the results are provided in Table 1 and Table 2.

4.1.1 [^{14}C]-Propiconazole in formulation concentrate (125 g/L) in human split-thickness skin membranes

A total of 16 samples of human split-thickness skin membranes obtained from 8 different donors were dosed topically with [^{14}C]-Propiconazole in the formulation concentrate (125 g/L). Cells 1, 2, 3 and 5 were excluded due to low mass balance. Overall, the absorption profiles looked similar for all samples. Absorption calculated throughout the experiment was above the limit of reliable measurement (LoRM) from 4 h post dose for all cells. The individual absorption profiles are provided in Figure 1. The individual absorption profiles excluding Cells 1, 2, 3 and 5 is provided in Figure 2. The mass balance for all individual samples was within 100 ± 10%. The following results are provided as mean values (n = 12).

The mean absorption rate of [^{14}C]-Propiconazole from the formulation concentrate through human split-thickness skin was 0.31 µg equiv./cm^2/h during the 24 h experimental period. The amount penetrated at 24 h, as measured in the receptor fluid, was 7.47 µg equiv./cm^2 (0.59% of the applied dose).

Following the skin wash at 6 h, 94.46% of the applied dose of [^{14}C]-Propiconazole was washed off. At 24 h post dose, a further 0.76% was removed during the skin wash. A proportion of the dose applied was recovered from the donor chamber wash (0.12%), exposed skin (0.26%) and receptor chamber wash (0.06%). The mean total recovery was 96.39% of the applied dose.

The distribution of radioactivity is provided in Table 5. The absorption profile is provided in Table 6 and Figure 3. The distribution, by mass, of [^{14}C]-Propiconazole at 24 h post dose is shown in Table 7. The absorption profile, by mass, is provided in Table 8 and Figure 4. The distribution of radioactivity in the *stratum corneum*, by mass, is provided in Table 9 and Figure 5.

4.1.2 [^{14}C]-Propiconazole in spray dilution 1 (6.25 g/L) in human split-thickness skin membranes

A total of 16 samples of human split-thickness skin membranes obtained from 8 different donors were dosed topically with [^{14}C]-Propiconazole in spray dilution 1 (6.25 g/L). Cells 12 and 15 were excluded due to low mass balance. Overall, the absorption profiles looked similar for all samples. Absorption calculated throughout the experiment was above the LoRM from 2 h post dose for all cells. The individual absorption profiles are provided in

Figure 6. The individual absorption profiles excluding Cells 12 and 15 is provided in Figure 7. The mass balance for all individual samples was within 100 ± 10%. The following results are provided as mean values (n = 14).

The mean absorption rate of [^{14}C]-Propiconazole from spray dilution 1 through human split-thickness skin was 0.16 µg equiv./cm^2/h during the 24 h experimental period. The amount penetrated at 24 h, as measured in the receptor fluid, was 3.92 µg equiv./cm^2 (6.34% of the applied dose).

Following the skin wash at 6 h, 80.78% of the applied dose of [^{14}C]-Propiconazole was washed off. At 24 h post dose, a further 4.18% was removed with the skin wash. A proportion of the dose applied was recovered from the donor chamber wash (0.81%), exposed skin (1.88%) and receptor chamber wash (0.51%). The mean total recovery was 95.08% of the applied dose.

The distribution of radioactivity is provided in Table 10. The absorption profile is provided in Table 11 and Figure 8. The distribution, by mass, of [^{14}C]-Propiconazole at 24 h post dose is shown in Table 12. The absorption profile, by mass, is provided in Table 13 and Figure 9. The distribution of radioactivity in the *stratum corneum*, by mass, is provided in Table 14 and Figure 10.

4.1.3 [^{14}C]-Propiconazole in spray dilution 2 (0.625 g/L) in human split-thickness skin membranes

A total of 8 samples of human split-thickness skin membranes obtained from 4 different donors were dosed topically with [^{14}C]-Propiconazole in spray dilution 2 (0.625 g/L). Cell 20 was excluded due to low mass balance. Overall, the absorption profiles looked similar for all samples. Absorption calculated throughout the experiment was above the LoRM from 2 h post dose for all cells. The individual absorption profiles are provided in Figure 11. The individual absorption profiles excluding Cell 20 is provided in Figure 12. The mass balance for all individual samples was within 100 ± 10%. The following results are provided as mean values (n = 7).

The mean absorption rate of [^{14}C]-Propiconazole from spray dilution 2 through human split-thickness skin was 0.04 µg equiv./cm^2/h during the 24 h experimental period. The amount penetrated at 24 h, as measured in the receptor fluid, was 0.88 µg equiv./cm^2 (13.28% of the applied dose).

Following the skin wash at 6 h, 68.24% of the applied dose of [^{14}C]-Propiconazole was washed off. At 24 h post dose, a further 6.40% was removed with the skin wash. A proportion of the dose applied was recovered from the donor chamber wash (1.10%), exposed skin (3.99%) and receptor chamber wash (0.81%). The mean total recovery was 94.91% of the applied dose.

The distribution of radioactivity is provided in Table 15. The absorption profile is provided in Table 16 and Figure 13. The distribution, by mass, of [^{14}C]-Propiconazole at 24 h post dose is shown in Table 17. The absorption profile, by mass, is provided in Table 18 and Figure 14. The distribution of radioactivity in the *stratum corneum*, by mass, is provided in Table 19 and Figure 15.

4.2 [^{14}C]-Fenpropidin in the Formulation Concentrate, Spray Dilution 1 and Spray Dilution 2

A summary of the results are provided in Table 3 and Table 4.

4.2.1 [^{14}C]-Fenpropidin in formulation concentrate (275 g/L) in human split-thickness skin membranes

A total of 16 samples of human split-thickness skin membranes obtained from 8 different donors were dosed topically with [^{14}C]-Fenpropidin in the formulation concentrate (275 g/L). Cells 27 and 32 were excluded due to low mass balance. Overall, the absorption profiles looked similar for all samples. Absorption calculated throughout the experiment was above the LoRM from 6 h post dose for all cells. The individual absorption profiles are provided in Figure 16. The individual absorption profiles excluding Cells 27 and 32 is provided in Figure 17. The mass balance for all individual samples was within 100 ± 10%. The following results are provided as mean values (n = 14).

The mean absorption rate of [^{14}C]-Fenpropidin from the formulation concentrate through human split-thickness skin was 1.17 µg equiv./cm^2/h during the 24 h experimental period. The amount penetrated at 24 h, as measured in the receptor fluid, was 28.2 µg equiv./cm^2 (1.02% of the applied dose).

Following the skin wash at 6 h, 92.55% of the applied dose of [^{14}C]-Fenpropidin was washed off. At 24 h post dose, a further 1.16% was removed during the skin wash. A proportion of the dose applied was recovered from the donor chamber wash (0.19%), exposed skin (0.47%) and receptor chamber wash (0.08%). The mean total recovery was 95.74% of the applied dose.

The distribution of radioactivity is provided in Table 20. The absorption profile is provided in Table 21 and Figure 18. The distribution, by mass, of [^{14}C]-Fenpropidin at 24 h post dose is shown in Table 22. The absorption profile, by mass, is provided in Table 23 and Figure 19. The distribution of radioactivity in the *stratum corneum*, by mass, is provided in Table 24 and Figure 20.

4.2.2 [^{14}C]-Fenpropidin in spray dilution 1 (13.75 g/L) in human split-thickness skin membranes

A total of 8 samples of human split-thickness skin membranes obtained from 4 different donors were dosed topically with [^{14}C]-Fenpropidin in spray dilution 1 (13.75 g/L). Overall,

the absorption profiles looked similar for all samples. Absorption calculated throughout the experiment was above the LoRM from 4 h post dose for all cells. The individual absorption profiles are provided in Figure 21. The mass balance for all individual samples was within 100 ± 10%. The following results are provided as mean values (n = 8).

The mean absorption rate of [^{14}C]-Fenpropidin from spray dilution 1 through human split-thickness skin was 0.42 µg equiv./cm^2/h during the 24 h experimental period. The amount penetrated at 24 h, as measured in the receptor fluid, was 10.1 µg equiv./cm^2 (6.83% of the applied dose).

Following the skin wash at 6 h, 79.88% of the applied dose of [^{14}C]-Fenpropidin was washed off. A proportion of the dose applied was recovered from the 6 h filter (0.32%). At 24 h post dose, a further 3.07% was removed with the skin wash. A proportion of the dose applied was recovered from the donor chamber wash/trap (0.52%), 24 h filter (0.27%), exposed skin (2.48%) and receptor chamber wash (0.44%). The mean total recovery was 95.13% of the applied dose.

The distribution of radioactivity is provided in Table 25. The absorption profile is provided in Table 26 and Figure 22. The distribution, by mass, of [^{14}C]-Fenpropidin at 24 h post dose is shown in Table 27. The absorption profile, by mass, is provided in Table 28 and Figure 23. The distribution of radioactivity in the *stratum corneum*, by mass, is provided in Table 29 and Figure 24.

4.2.3 [^{14}C]-Fenpropidin in spray dilution 2 (1.375 g/L) in human split-thickness skin membranes

A total of 8 samples of human split-thickness skin membranes obtained from 4 different donors were dosed topically with [^{14}C]-Fenpropidin in spray dilution 2 (1.375 g/L). Cell 47 was excluded due to low mass balance. Overall, the absorption profiles looked similar for all samples. Absorption calculated throughout the experiment was above the LoRM from 4 h post dose for all cells. The individual absorption profiles are provided in Figure 25. The individual absorption profiles excluding Cell 47 is provided in Figure 26. The mass balance for all individual samples was within 100 ± 10%. The following results are provided as mean values (n = 7).

The mean absorption rate of [^{14}C]-Fenpropidin from spray dilution 2 through human split-thickness skin was 0.07 µg equiv./cm^2/h during the 24 h experimental period. The amount penetrated at 24 h, as measured in the receptor fluid, was 1.59 µg equiv./cm^2 (11.10% of the applied dose).

Following the skin wash at 6 h, 71.21% of the applied dose of [^{14}C]-Fenpropidin was washed off. A proportion of the dose applied was recovered from the 6 h filter (1.37%). At 24 h post dose, a further 4.66% was removed with the skin wash. A proportion of the dose applied was recovered from the donor chamber wash/trap (1.13%), 24 h filter (0.70%), exposed skin

(2.81%) and receptor chamber wash (0.67%). The mean total recovery was 95.04% of the applied dose.

The distribution of radioactivity is provided in Table 30. The absorption profile is provided in Table 31 and Figure 27. The distribution, by mass, of [^{14}C]-Fenpropidin at 24 h post dose is shown in Table 32. The absorption profile, by mass, is provided in Table 33 and Figure 28. The distribution of radioactivity in the *stratum corneum*, by mass, is provided in Table 34 and Figure 29.

4.3 Post Dose Washing Efficiency (6 h)

4.3.1 Propiconazole

Overall, most of the applied dose recovered in tissue swabs 1-5 was removed with tissue swab 1. Thereafter, there was a general decrease in the percentage of the applied dose removed with tissue swabs 2-5. In the final tissue swab of the Formulation Concentrate, Spray Dilution 1, and Spray Dilution 2, a mean of 0.08-0.13% of the applied dose was detected, indicating that the washing process was efficient at removing the applied dose. The amount of radioactivity (% applied dose and µg equiv./cm^2) in each tissue swab following application of the formulation concentrate, spray dilution 1 and spray dilution 2 is presented in Table 35.

4.3.2 Fenpropidin

Overall, most of the applied dose recovered in tissue swabs 1-5 was removed with tissue swab 1. Thereafter, there was a general decrease in the percentage of the applied dose removed with tissue swabs 2-5. In the final tissue swab of the Formulation Concentrate, Spray Dilution 1, and Spray Dilution 2, a mean of 0.14-0.29% of the applied dose was detected, indicating that the washing process was efficient at removing the applied dose. The amount of radioactivity (% applied dose and µg equiv./cm^2) in each tissue swab following application of the formulation concentrate, spray dilution 1 and spray dilution 2 is presented in Table 36.

5.0 CONCLUSIONS

The study demonstrated that the amount of propiconazole absorbed through human split-thickness skin membranes over 24 h (following a 6 h exposure) from the formulation concentrate (125 g/L) and the intended in-use concentrations (6.25 g/L and 0.625 g/L) was 0.64%, 6.85%, and 14.09% of the applied dose, respectively, as measured in the receptor fluid and receptor chamber wash. The study demonstrated that the amount of fenpropidin absorbed through human split-thickness skin membranes over 24 h (following a 6 h exposure) from the formulation concentrate (275 g/L) and the intended in-use concentrations (13.75 g/L and 1.375 g/L) was 1.10%, 7.28%, and 11.77% of the applied dose, respectively, as measured in the receptor fluid and receptor chamber wash.

6.0 REFERENCES

1. Page, L (2020). Inter Laboratory Comparison of The *In Vitro* Percutaneous Absorption of Radiolabelled Caffeine Through Human Split-Thickness Skin. Charles River Study No. 997161.
2. Whitson, S (2020). Creation of New Barrier Integrity Rejection Criteria Using Historical Data. Charles River Study No. 996419.
3. The Pesticide Manual, 16th Edition, BCPC, 7 Omni Business, Omega Park, Alton, Hampshire, GU34 2QD, UK.

TABLES SECTION

TABLE 1 Summary of Propiconazole Distribution in Human Split-Thickness Membranes

Test Preparation	Formulation Concentrate (125 g/L)	Spray Dilution 1 (6.25 g/L)	Spray Dilution 2 (0.625 g/L)
Test Item	Propiconazole		
Distribution	% Applied Dose	% Applied Dose	% Applied Dose
Dislodgeable Dose 6 h*	94.46	80.78	68.24
Dislodgeable Dose 24 h**	0.76	4.18	6.40
Donor Chamber Wash	0.12	0.81	1.10
Total Dislodgeable Dose***	95.34	85.77	75.74
Tape Strips 1-2	0.04	0.15	0.20
Tape Strips 3-20	0.09	0.42	0.82
Unexposed Skin	<0.01	0.02	0.06
Exposed Skin	0.26	1.88	3.99
Receptor Fluid	0.59	6.34	13.28
Receptor Chamber Wash	0.06	0.51	0.81
Mass Balance	96.39	95.08	94.91
Distribution	µg equiv./cm^2	µg equiv./cm^2	µg equiv./cm^2
Dislodgeable Dose 6 h*	1204	49.9	4.53
Dislodgeable Dose 24 h**	9.70	2.59	0.43
Donor Chamber Wash	1.56	0.51	0.07
Total Dislodgeable Dose***	1215	53.0	5.03
Tape Strips 1-2	0.57	0.09	0.01
Tape Strips 3-20	1.09	0.26	0.05
Unexposed Skin	0.05	0.01	<0.01
Exposed Skin	3.35	1.16	0.27
Receptor Fluid	7.47	3.92	0.88
Receptor Chamber Wash	0.74	0.31	0.05
Mass Balance	1229	58.7	6.31

* Dislodgeable Dose 6 h = Skin Wash 6 h + Tissue Swab 6 h + Pipette Tip 6 h
** Dislodgeable Dose 24 h = Skin Wash 24 h + Tissue Swab 24 h + Pipette Tip 24 h
** Total Dislodgeable Dose = Dislodgeable Dose 6 h + Dislodgeable Dose 24 h + Donor Chamber Wash

TABLE 2 **Summary of Propiconazole Absorption through Human Split-Thickness Membranes**

Application of Test Materials and Actual Concentration of Dose Preparation	Mean Absorption Rates	
	Time Period (h)	Absorption Rate
Formulation Concentrate		µg equiv./cm^2/h ± SD
(125 g/L propiconazole)	0-2	0.02 ± <0.01
10.00 µL/cm^2 (1274 ai/cm^2 for cells 1-8, 1275 ai/cm^2 for cells 69-76)	2-6	0.22 ± 0.05
Unoccluded	6-24	0.36 ± 0.06
Duration of experiment: 24 h, n = 12	0-24	0.31 ± 0.05
Spray Dilution 1		µg equiv./cm^2/h ± SD
(6.25 g/L propiconazole)	0-2	0.07 ± 0.02
10.00 µL/cm^2 (65.0 ai/cm^2 for cells 9-16, 59.4 ai/cm^2 for cells 77-84)	2-6	0.27 ± 0.04
Unoccluded	6-24	0.15 ± 0.02
Duration of experiment: 24 h, n = 14	0-24	0.16 ± 0.02
Spray Dilution 2		µg equiv./cm^2/h ± SD
(0.625 g/L propiconazole)	0-2	0.03 ± 0.01
10.00 µL/cm^2 (6.64 ai/cm^2)	2-6	0.07 ± 0.02
Unoccluded	6-24	0.03 ± 0.01
Duration of experiment: 24 h, n = 7	0-24	0.04 ± 0.01

TABLE 3 Summary of Fenpropidin Distribution in Human Split-Thickness Membranes

Test Preparation	Formulation Concentrate (275 g/L)	Spray Dilution 1 (13.75 g/L)	Spray Dilution 2 (1.375 g/L)
Test Item	Fenpropidin		
Distribution	% Applied Dose	% Applied Dose	% Applied Dose
Dislodgeable Dose 6 h*	92.55	80.20	72.58
Dislodgeable Dose 24 h**	1.16	3.34	5.36
Donor Chamber/Trap Wash	0.19	0.52	1.13
Filters 6 h	N/A	0.32	1.37
Filters 24 h	N/A	0.27	0.70
Total Dislodgeable Dose***	93.91	84.06	79.08
Tape Strips 1-2	0.12	0.19	0.34
Tape Strips 3-20	0.13	0.38	0.47
Unexposed Skin	0.01	0.75	0.70
Exposed Skin	0.47	2.48	2.81
Receptor Fluid	1.02	6.83	11.10
Receptor Chamber Wash	0.08	0.44	0.67
Mass Balance	95.74	95.13	95.04
Distribution	µg equiv./cm^2	µg equiv./cm^2	µg equiv./cm^2
Dislodgeable Dose 6 h*	2544	118	10.4
Dislodgeable Dose 24 h**	32.0	4.91	0.77
Donor Chamber/Trap Wash	5.32	0.76	0.16
Filters 6 h	N/A	0.47	0.20
Filters 24 h	N/A	0.40	0.10
Total Dislodgeable Dose***	2581	124	11.4
Tape Strips 1-2	3.29	0.28	0.05
Tape Strips 3-20	3.63	0.55	0.07
Unexposed Skin	0.25	1.11	0.10
Exposed Skin	12.9	3.65	0.40
Receptor Fluid	28.2	10.1	1.59
Receptor Chamber Wash	2.11	0.65	0.10
Mass Balance	2632	140	13.6

* Dislodgeable Dose 6 h = Skin Wash 6 h + Tissue Swab 6 h + Pipette Tip 6 h + Filters 6 h
** Dislodgeable Dose 24 h = Skin Wash 24 h + Tissue Swab 24 h + Pipette Tip 24 h + Filters 24 h
*** Total Dislodgeable Dose = Dislodgeable Dose 6 h + Dislodgeable Dose 24 h + Donor Chamber Wash

TABLE 4 **Summary of Fenpropidin Absorption through Human Split-Thickness Membranes**

Application of Test Materials and Actual Concentration of Dose Preparation	Mean Absorption Rates	
	Time Period (h)	Absorption Rate
Formulation Concentrate		µg equiv./cm^2/h ± SD
(275 g/L fenpropidin)	0-2	0.10 ± 0.03
10.00 µL/cm^2 (2749 ai/cm^2 for cells 25-32, 2748 ai/cm^2 for cells 61-68)	2-6	1.13 ± 0.24
Unoccluded	6-24	1.30 ± 0.18
Duration of experiment: 24 h, n = 14	0-24	1.17 ± 0.16
Spray Dilution 1		µg equiv./cm^2/h ± SD
(13.75 g/L fenpropidin)	0-2	0.09 ± 0.03
10.00 µL/cm^2 (147 ai/cm^2)	2-6	0.72 ± 0.15
Occluded	6-24	0.39 ± 0.11
Duration of experiment: 24 h, n = 8	0-24	0.42 ± 0.11
Spray Dilution 2		µg equiv./cm^2/h ± SD
(1.375 g/L fenpropidin)	0-2	0.04 ± 0.01
10.00 µL/cm^2 (14.4 ai/cm^2)	2-6	0.14 ± 0.02
Occluded	6-24	0.05 ± 0.01
Duration of experiment: 24 h, n = 7	0-24	0.07 ± 0.01

TABLE 5 **Distribution of Radioactivity (% Applied Dose) at 24 h Post Dose Following Topical Application of [^{14}C]-Propiconazole in Formulation Concentrate (125 g/L) to Human Split-Thickness Membranes**

	Cell Number and Donor Number							
	Cell 1 (1357)	*Cell 2 (1357)*	*Cell 3 (1382)*	Cell 4 (1382)	*Cell 5 (1368)*	Cell 6 (1368)	Cell 7 (1472)	Cell 8 (1472)
Skin Wash 6 h	*10.14*	*17.12*	*31.56*	11.99	*29.33*	34.73	15.73	39.51
Tissue Swab 6 h	*76.46*	*46.51*	*36.58*	83.44	*56.59*	59.93	76.46	56.43
Pipette Tip 6 h	*0.14*	*0.15*	*0.38*	0.16	*0.16*	0.25	0.16	0.23
Skin Wash 24 h	*0.31*	*0.52*	*0.68*	0.20	*0.52*	0.52	0.42	0.72
Tissue Swab 24 h	*0.07*	*0.17*	*0.38*	0.04	*0.26*	0.55	0.06	0.69
Pipette Tip 24 h	**0.00*	*0.00*	**0.00*	*0.00	**0.00*	*0.00	*0.00	*0.00
Donor Chamber Wash	*0.02*	*0.09*	*0.14*	0.18	*0.29*	0.19	0.02	0.14
Stratum Corneum 1-2	*0.01*	*0.03*	*0.02*	0.02	*0.04*	0.03	0.02	0.12
Stratum Corneum 3-5	*0.00*	*0.01*	*0.01*	0.01	*0.02*	0.02	0.02	0.11
Stratum Corneum 6-10	*0.00*	*0.02*	*0.01*	0.01	*0.02*	0.02	0.03	0.06
Stratum Corneum 11-15	*0.00*	*0.01*	*0.01*	0.00	*0.01*	0.01	0.02	0.10
Stratum Corneum 16-20	*0.00*	*0.01*	*0.01*	0.00	*0.01*	0.01	0.01	0.07
Unexposed Skin	**0.00*	**0.00*	*0.00*	*0.00	*0.00*	0.00	0.00	0.02
Exposed Skin	*0.23*	*0.20*	*0.31*	0.15	*0.44*	0.24	0.08	0.37
Receptor Fluid	*0.36*	*0.85*	*0.90*	0.51	*0.65*	0.49	0.20	0.31
Receptor Chamber Wash	*0.03*	*0.06*	*0.09*	0.04	*0.04*	0.03	*0.02	0.07
Mass Balance	*87.79*	*65.75*	*71.09*	96.73	*88.38*	96.99	93.25	98.94

Cells 1, 2, 3 and 5 were excluded due to low mass balance
*=Results calculated from data less than 30 d.p.m. above background

	Cell Number and Donor Number									
	Cell 69 (1370)	Cell 70 (1370)	Cell 71 (1445)	Cell 72 (1445)	Cell 73 (1344)	Cell 74 (1344)	Cell 75 (1449)	Cell 76 (1449)	Mean	SD
Skin Wash 6 h	26.20	42.48	43.41	15.17	46.85	21.93	46.05	63.10	33.93	15.75
Tissue Swab 6 h	65.88	52.01	53.66	78.50	45.92	71.35	51.19	30.49	60.44	15.34
Pipette Tip 6 h	0.02	0.05	0.16	0.03	0.02	0.01	0.05	0.02	0.10	0.09
Skin Wash 24 h	0.45	0.62	0.56	0.33	0.16	0.51	0.70	0.11	0.44	0.20
Tissue Swab 24 h	0.40	0.45	0.30	0.35	0.06	0.24	0.60	0.06	0.32	0.23
Pipette Tip 24 h	0.00	*0.00	*0.00	0.00	*0.00	0.00	0.00	*0.00	°0.00	°0.00
Donor Chamber Wash	0.11	0.15	0.05	0.05	0.02	0.03	0.41	0.12	0.12	0.11
Stratum Corneum 1-2	0.19	0.11	0.01	0.00	0.01	0.01	0.02	0.00	0.04	0.06
Stratum Corneum 3-5	0.08	0.08	0.01	0.00	0.01	0.01	0.02	0.00	0.03	0.04
Stratum Corneum 6-10	0.05	0.05	0.01	0.01	0.01	0.02	0.01	0.01	0.02	0.02
Stratum Corneum 11-15	0.02	0.02	0.01	0.01	0.01	0.02	0.01	0.00	0.02	0.03
Stratum Corneum 16-20	0.01	0.01	0.01	0.00	0.00	0.02	0.01	0.00	0.01	0.02
Unexposed Skin	0.00	0.00	0.01	0.00	0.00	0.00	*0.00	0.00	°0.00	°0.00
Exposed Skin	0.17	0.16	0.56	0.46	0.24	0.43	0.18	0.10	0.26	0.16
Receptor Fluid	0.40	0.56	0.68	0.75	0.99	1.47	0.37	0.31	0.59	0.36
Receptor Chamber Wash	0.04	0.04	0.05	0.11	0.09	0.13	0.07	*0.02	°0.06	°0.03
Mass Balance	94.02	96.78	99.50	95.78	94.39	96.18	99.71	94.36	96.39	2.17

*=Results calculated from data less than 30 d.p.m. above background
°=Mean includes results calculated from data less than 30 d.p.m above background

TABLE 6 **Cumulative Absorption (% Applied Dose) of [^{14}C]-Propiconazole into Receptor Fluid Following Topical Application of the [^{14}C]-Propiconazole in Formulation Concentrate (125 g/L) to Human Split-Thickness Membranes**

	Cell Number and Donor Number							
Time (h)	*Cell 1 (1357)*	*Cell 2 (1357)*	*Cell 3 (1382)*	Cell 4 (1382)	*Cell 5 (1368)*	Cell 6 (1368)	Cell 7 (1472)	Cell 8 (1472)
0	*0.00*	*0.00*	*0.00*	0.00	*0.00*	0.00	0.00	0.00
2	**0.00*	**0.01*	**0.00*	*0.00	**0.01*	*0.00	*0.00	*0.00
4	**0.02*	*0.05*	*0.03*	*0.02	*0.03*	0.03	*0.01	*0.00
6	*0.06*	*0.14*	*0.09*	0.05	*0.08*	0.07	0.03	*0.01
8	*0.11*	*0.29*	*0.19*	0.14	*0.18*	0.17	0.06	0.03
12	*0.21*	*0.51*	*0.38*	0.29	*0.33*	0.28	0.12	0.09
24	*0.36*	*0.85*	*0.90*	0.51	*0.65*	0.49	0.20	0.31

	Cell Number and Donor Number									
Time (h)	Cell 69 (1370)	Cell 70 (1370)	Cell 71 (1445)	Cell 72 (1445)	Cell 73 (1344)	Cell 74 (1344)	Cell 75 (1449)	Cell 76 (1449)	Mean	SD
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2	*0.00	*0.00	*0.01	*0.00	*0.00	*0.01	*0.01	*0.00	°0.00	°0.00
4	*0.02	*0.01	*0.01	*0.02	0.03	0.06	*0.02	*0.01	°0.02	°0.01
6	0.05	0.06	0.06	0.08	0.16	0.19	0.07	0.03	°0.07	°0.05
8	0.09	0.12	0.12	0.16	0.27	0.34	0.12	0.07	0.14	0.09
12	0.20	0.26	0.29	0.36	0.58	0.70	0.24	0.16	0.30	0.18
24	0.40	0.56	0.68	0.75	0.99	1.47	0.37	0.31	0.59	0.36

Cells 1, 2, 3 and 5 were excluded due to low mass balance
*=Results calculated from data less than 30 d.p.m. above background
°=Mean includes results calculated from data less than 30 d.p.m above background

TABLE 7 **Distribution of Radioactivity (µg equiv./cm^2) at 24 h Post Dose Following Topical Application of [^{14}C]-Propiconazole in Formulation Concentrate (125 g/L) to Human Split-Thickness Membranes**

	Cell Number and Donor Number							
	Cell 1 (1357)	*Cell 2 (1357)*	*Cell 3 (1382)*	Cell 4 (1382)	*Cell 5 (1368)*	Cell 6 (1368)	Cell 7 (1472)	Cell 8 (1472)
Skin Wash 6 h	*129.13*	*218.16*	*402.06*	152.71	*373.71*	442.43	200.40	503.41
Tissue Swab 6 h	*974.17*	*592.56*	*466.03*	1063.05	*720.94*	763.51	974.20	719.00
Pipette Tip 6 h	*1.82*	*1.91*	*4.83*	1.98	*2.02*	3.15	2.09	2.88
Skin Wash 24 h	*3.93*	*6.57*	*8.63*	2.55	*6.63*	6.61	5.38	9.13
Tissue Swab 24 h	*0.94*	*2.12*	*4.88*	0.47	*3.38*	6.98	0.81	8.83
Pipette Tip 24 h	**0.00*	*0.02*	**0.00*	*0.00	**0.01*	*0.00	*0.00	0.01
Donor Chamber Wash	*0.29*	*1.13*	*1.82*	2.26	*3.70*	2.43	0.25	1.73
Stratum Corneum 1-2	*0.08*	*0.32*	*0.28*	0.21	*0.50*	0.40	0.25	1.51
Stratum Corneum 3-5	*0.05*	*0.16*	*0.13*	0.09	*0.21*	0.25	0.21	1.44
Stratum Corneum 6-10	*0.03*	*0.22*	*0.15*	0.09	*0.20*	0.19	0.32	0.82
Stratum Corneum 11-15	*0.03*	*0.19*	*0.09*	0.05	*0.15*	0.09	0.23	1.30
Stratum Corneum 16-20	*0.03*	*0.09*	*0.08*	0.05	*0.13*	0.09	0.11	0.83
Unexposed Skin	**0.02*	**0.00*	*0.05*	*0.00	*0.03*	0.02	0.05	0.23
Exposed Skin	*2.88*	*2.59*	*3.99*	1.95	*5.62*	3.04	0.99	4.71
Receptor Fluid	*4.64*	*10.87*	*11.51*	6.51	*8.22*	6.20	2.51	3.93
Receptor Chamber Wash	*0.41*	*0.76*	*1.19*	0.46	*0.56*	0.38	*0.21	0.84
Mass Balance	*1118.45*	*837.67*	*905.71*	1232.43	*1126.01*	1235.79	1188.01	1260.62

Cells 1, 2, 3 and 5 were excluded due to low mass balance
*=Results calculated from data less than 30 d.p.m. above background

	Cell Number and Donor Number									
	Cell 69 (1370)	Cell 70 (1370)	Cell 71 (1445)	Cell 72 (1445)	Cell 73 (1344)	Cell 74 (1344)	Cell 75 (1449)	Cell 76 (1449)	Mean	SD
Skin Wash 6 h	334.03	541.61	553.54	193.44	597.35	279.65	587.23	804.60	432.53	200.82
Tissue Swab 6 h	840.10	663.19	684.25	1001.00	585.55	909.74	652.69	388.77	770.42	195.38
Pipette Tip 6 h	0.30	0.60	2.04	0.32	0.19	0.07	0.67	0.27	1.21	1.13
Skin Wash 24 h	5.69	7.93	7.11	4.23	2.02	6.56	8.93	1.46	5.63	2.60
Tissue Swab 24 h	5.11	5.76	3.87	4.48	0.80	3.02	7.64	0.82	4.05	2.92
Pipette Tip 24 h	0.04	*0.00	*0.00	0.05	*0.00	0.02	0.06	*0.00	°0.02	°0.02
Donor Chamber Wash	1.36	1.94	0.70	0.59	0.30	0.35	5.28	1.53	1.56	1.40
Stratum Corneum 1-2	2.40	1.41	0.08	0.05	0.07	0.11	0.28	0.04	0.57	0.77
Stratum Corneum 3-5	1.07	1.04	0.10	0.05	0.09	0.19	0.27	0.05	0.40	0.49
Stratum Corneum 6-10	0.68	0.58	0.13	0.09	0.13	0.29	0.14	0.07	0.29	0.26
Stratum Corneum 11-15	0.21	0.19	0.12	0.07	0.07	0.28	0.15	0.06	0.23	0.34
Stratum Corneum 16-20	0.09	0.09	0.18	0.05	0.06	0.20	0.12	0.06	0.16	0.22
Unexposed Skin	0.05	0.06	0.08	0.02	0.02	0.03	*0.00	0.02	°0.05	°0.06
Exposed Skin	2.21	2.05	7.20	5.92	3.08	5.45	2.32	1.28	3.35	1.99
Receptor Fluid	5.04	7.09	8.72	9.54	12.60	18.80	4.76	3.94	7.47	4.53
Receptor Chamber Wash	0.52	0.53	0.64	1.37	1.20	1.60	0.86	*0.28	°0.74	°0.44
Mass Balance	1198.87	1234.09	1268.76	1221.28	1203.52	1226.36	1271.39	1203.26	1228.70	27.68

*=Results calculated from data less than 30 d.p.m. above background
°=Mean includes results calculated from data less than 30 d.p.m above background

TABLE 8 **Cumulative Absorption (µg equiv./cm^2) of [^{14}C]-Propiconazole into Receptor Fluid Following Topical Application of [^{14}C]-Propiconazole in Formulation Concentrate (125 g/L) to Human Split-Thickness Membranes**

	Cell Number and Donor Number							
Time (h)	*Cell 1 (1357)*	*Cell 2 (1357)*	*Cell 3 (1382)*	Cell 4 (1382)	*Cell 5 (1368)*	Cell 6 (1368)	Cell 7 (1472)	Cell 8 (1472)
0	*0.00*	*0.00*	*0.00*	0.00	*0.00*	0.00	0.00	0.00
2	**0.03*	**0.14*	**0.01*	*0.05	**0.07*	*0.05	*0.04	*0.04
4	**0.20*	*0.63*	*0.38*	*0.29	*0.40*	0.37	0.16	*0.04
6	*0.71*	*1.84*	*1.21*	0.70	*1.05*	0.93	0.33	*0.16
8	*1.44*	*3.64*	*2.38*	1.80	*2.27*	2.19	0.75	0.43
12	*2.69*	*6.52*	*4.80*	3.73	*4.24*	3.54	1.50	1.11
24	*4.64*	*10.87*	*11.51*	6.51	*8.22*	6.20	2.51	3.93

	Cell Number and Donor Number									
Time (h)	Cell 69 (1370)	Cell 70 (1370)	Cell 71 (1445)	Cell 72 (1445)	Cell 73 (1344)	Cell 74 (1344)	Cell 75 (1449)	Cell 76 (1449)	Mean	SD
0	*0.00	*0.00	*0.00	*0.00	*0.00	*0.00	*0.00	*0.00	°0.00	°0.00
2	*0.01	*0.00	*0.09	*0.04	0.06	0.08	*0.06	*0.04	°0.05	°0.03
4	0.21	0.17	0.18	0.21	0.43	0.72	0.24	0.11	°0.26	°0.18
6	0.69	0.74	0.82	1.06	2.10	2.39	0.85	0.38	0.93	0.67
8	1.20	1.55	1.50	2.03	3.39	4.27	1.54	0.93	1.80	1.09
12	2.53	3.28	3.69	4.64	7.46	8.87	3.04	2.07	3.79	2.29
24	5.04	7.09	8.72	9.54	12.60	18.80	4.76	3.94	7.47	4.53

Cells 1, 2, 3 and 5 were excluded due to low mass balance
*=Results calculated from data less than 30 d.p.m. above background
°=Mean includes results calculated from data less than 30 d.p.m above background

TABLE 9 **Distribution of Radioactivity (µg equiv./cm^2) in the *Stratum Corneum* at 24 h Post Dose Following Topical Application of [^{14}C]-Propiconazole in Formulation Concentrate (125 g/L) to Human Split-Thickness Membranes**

	Cell Number and Donor Number							
Tape Strip No.	*Cell 1 (1357)*	*Cell 2 (1357)*	*Cell 3 (1382)*	Cell 4 (1382)	*Cell 5 (1368)*	Cell 6 (1368)	Cell 7 (1472)	Cell 8 (1472)
1	*0.03*	*0.26*	*0.22*	0.17	*0.35*	0.30	0.17	1.13
2	*0.04*	*0.06*	*0.07*	0.04	*0.15*	0.10	0.08	0.38
3	**0.02*	*0.04*	*0.05*	0.03	*0.11*	0.12	0.07	0.61
4	**0.02*	*0.06*	*0.04*	0.03	*0.05*	0.09	0.07	0.46
5	**0.02*	*0.06*	*0.04*	0.03	*0.04*	0.04	0.06	0.37
6	*0.02*	*0.04*	*0.05*	0.03	*0.04*	0.04	0.04	0.27
7	**0.01*	*0.06*	*0.02*	*0.02	*0.05*	0.07	0.06	0.19
8	**0.00*	*0.05*	*0.02*	0.02	*0.03*	0.03	0.10	0.15
9	**0.00*	*0.04*	**0.01*	*0.01	*0.04*	0.02	0.07	0.08
10	**0.00*	*0.02*	*0.04*	*0.01	*0.05*	0.04	0.06	0.12
11	**0.01*	*0.04*	*0.03*	*0.01	*0.03*	0.03	0.06	0.37
12	**0.01*	*0.06*	*0.02*	*0.01	*0.03*	*0.02	0.04	0.27
13	**0.00*	*0.05*	**0.01*	*0.01	*0.03*	*0.02	0.04	0.18
14	**0.01*	*0.02*	*0.02*	*0.01	*0.03*	*0.01	0.04	0.23
15	**0.01*	*0.02*	**0.01*	*0.01	*0.02*	*0.02	0.04	0.24
16	**0.01*	*0.03*	*0.02*	*0.01	*0.03*	0.02	0.03	0.19
17	**0.00*	*0.02*	*0.02*	*0.01	*0.02*	*0.01	*0.02	0.18
18	**0.01*	*0.02*	**0.01*	*0.01	*0.03*	*0.02	0.02	0.16
19	**0.01*	**0.01*	**0.01*	*0.01	*0.02*	*0.02	0.03	0.19
20	**0.01*	**0.01*	**0.01*	*0.01	*0.02*	0.02	*0.02	0.11

Cells 1, 2, 3 and 5 were excluded due to low mass balance
*=Results calculated from data less than 30 d.p.m. above background

Tape Strip No.	Cell Number and Donor Number									
	Cell 69 (1370)	Cell 70 (1370)	Cell 71 (1445)	Cell 72 (1445)	Cell 73 (1344)	Cell 74 (1344)	Cell 75 (1449)	Cell 76 (1449)	Mean	SD
1	1.53	0.77	0.03	0.03	0.04	0.05	0.18	0.03	0.37	0.50
2	0.86	0.65	0.05	0.02	0.03	0.06	0.10	*0.01	°0.20	°0.28
3	0.54	0.34	0.04	*0.02	0.02	0.08	0.15	0.02	°0.17	°0.21
4	0.30	0.46	0.03	*0.02	0.03	0.05	0.03	*0.01	°0.13	°0.17
5	0.22	0.23	0.03	*0.01	0.03	0.05	0.08	0.02	°0.10	°0.11
6	0.24	0.20	0.02	0.02	0.03	0.04	E.C.	*0.01	°0.09	°0.10
7	0.14	0.14	0.03	*0.01	0.03	0.06	*0.01	*0.01	°0.06	°0.06
8	0.13	0.09	0.03	0.02	0.03	0.05	0.02	*0.01	°0.06	°0.05
9	0.07	0.08	0.03	*0.02	0.02	0.05	0.06	*0.02	°0.04	°0.03
10	0.11	0.08	*0.01	*0.01	0.02	0.09	0.05	*0.02	°0.05	°0.04
11	0.06	0.05	0.03	0.02	*0.01	0.07	0.05	*0.01	°0.06	°0.10
12	0.05	0.04	*0.02	*0.01	0.02	0.07	0.02	*0.01	°0.05	°0.07
13	0.06	0.03	0.03	*0.01	*0.01	0.06	0.02	*0.01	°0.04	°0.05
14	0.03	0.05	0.03	*0.01	*0.01	0.04	*0.01	*0.01	°0.04	°0.06
15	0.02	0.03	0.02	0.03	*0.01	0.04	0.05	*0.02	°0.04	°0.06
16	*0.02	0.02	0.03	*0.01	*0.01	0.05	0.03	*0.01	°0.04	°0.05
17	0.02	0.03	0.02	*0.01	*0.02	0.05	0.02	*0.01	°0.03	°0.05
18	*0.02	*0.02	0.05	*0.01	*0.01	0.03	0.02	*0.01	°0.03	°0.04
19	0.02	*0.01	0.04	*0.02	*0.00	0.02	*0.01	*0.01	°0.03	°0.05
20	*0.01	*0.01	0.03	*0.01	*0.01	0.05	0.04	*0.01	°0.03	°0.03

E.C. = Epidermal Content
*=Results calculated from data less than 30 d.p.m. above background
°=Mean includes results calculated from data less than 30 d.p.m above background

TABLE 10 **Distribution of Radioactivity (% Applied Dose) at 24 h Post Dose Following Topical Application of [^{14}C]-Propiconazole in Spray Dilution 1 (6.25 g/L) to Human Split-Thickness Membranes**

	Cell Number and Donor Number							
	Cell 9 (1357)	Cell 10 (1357)	Cell 11 (1382)	*Cell 12 (1382)*	Cell 13 (1368)	Cell 14 (1368)	*Cell 15 (1472)*	Cell 16 (1472)
Skin Wash 6 h	33.65	23.96	38.20	*25.04*	20.64	33.86	*27.87*	17.76
Tissue Swab 6 h	48.23	53.00	44.10	*48.96*	58.08	41.79	*35.40*	60.04
Pipette Tip 6 h	0.14	0.22	0.04	*0.04*	0.15	0.09	*0.12*	0.21
Skin Wash 24 h	2.85	3.42	2.51	*1.21*	2.80	3.39	*2.03*	4.22
Tissue Swab 24 h	1.28	0.82	1.01	*0.74*	1.02	1.22	*1.20*	1.39
Pipette Tip 24 h	0.01	0.00	0.00	**0.00*	0.00	0.00	*0.00*	0.00
Donor Chamber Wash	0.43	0.07	0.73	*1.08*	1.22	4.92	*0.97*	0.28
Stratum Corneum 1-2	0.21	0.12	0.21	*0.20*	0.19	0.25	*0.11*	0.19
Stratum Corneum 3-5	0.10	0.08	0.09	*0.08*	0.11	0.19	*0.13*	0.20
Stratum Corneum 6-10	0.15	0.13	0.13	*0.07*	0.11	0.11	*0.20*	0.56
Stratum Corneum 11-15	0.10	0.07	0.10	*0.06*	0.06	0.09	*0.14*	0.26
Stratum Corneum 16-20	0.08	0.10	0.11	*0.03*	0.03	0.07	*0.12*	0.37
Unexposed Skin	0.02	0.03	0.02	*0.01*	0.03	0.01	*0.01*	0.03
Exposed Skin	2.13	2.82	1.14	*1.07*	2.21	1.79	*1.20*	1.63
Receptor Fluid	6.88	10.14	4.48	*4.59*	6.74	7.67	*2.12*	2.97
Receptor Chamber Wash	0.54	0.61	0.28	*0.27*	0.26	0.60	*0.27*	0.30
Mass Balance	96.78	95.58	93.14	*83.46*	93.66	96.05	*71.89*	90.43

Cells 12 and 15 were excluded due to low mass balance
*=Results calculated from data less than 30 d.p.m. above background

	Cell Number and Donor Number									
	Cell 77 (1370)	Cell 78 (1370)	Cell 79 (1445)	Cell 80 (1445)	Cell 81 (1344)	Cell 82 (1344)	Cell 83 (1449)	Cell 84 (1449)	Mean	SD
Skin Wash 6 h	28.62	28.71	38.81	30.57	39.28	46.69	32.21	44.27	32.66	8.44
Tissue Swab 6 h	52.07	51.90	40.87	46.54	39.03	33.99	54.44	48.31	48.03	7.49
Pipette Tip 6 h	0.02	0.03	0.02	0.12	0.03	0.03	0.10	0.08	0.09	0.07
Skin Wash 24 h	2.76	2.26	1.33	2.04	1.79	1.54	2.41	2.59	2.57	0.78
Tissue Swab 24 h	4.27	4.44	0.72	1.25	2.17	0.50	0.88	1.54	1.61	1.23
Pipette Tip 24 h	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	°0.00	°0.00
Donor Chamber Wash	0.17	0.19	0.16	0.62	0.18	0.16	1.23	0.95	0.81	1.25
Stratum Corneum 1-2	0.23	0.30	0.04	0.03	0.04	0.04	0.16	0.04	0.15	0.09
Stratum Corneum 3-5	0.12	0.23	0.04	0.03	0.04	0.05	0.13	0.07	0.11	0.06
Stratum Corneum 6-10	0.06	0.23	0.03	0.06	0.07	0.09	0.10	0.08	0.14	0.13
Stratum Corneum 11-15	0.04	0.13	0.02	0.06	0.06	0.09	0.11	0.06	0.09	0.06
Stratum Corneum 16-20	0.02	0.09	0.03	0.06	0.03	0.05	0.08	0.06	0.09	0.09
Unexposed Skin	0.02	0.03	0.05	0.03	0.02	0.00	0.02	0.00	0.02	0.01
Exposed Skin	0.25	2.23	2.78	3.04	2.12	1.65	1.24	1.25	1.88	0.76
Receptor Fluid	2.63	4.14	7.12	6.22	12.03	8.72	4.66	4.37	6.34	2.71
Receptor Chamber Wash	0.16	0.30	0.47	0.40	1.60	0.51	0.33	0.77	0.51	0.35
Mass Balance	91.47	95.23	92.50	91.08	98.49	94.13	98.10	104.42	95.08	3.68

°=Mean includes results calculated from data less than 30 d.p.m above background

TABLE 11 **Cumulative Absorption (% Applied Dose) of [^{14}C]-Propiconazole into Receptor Fluid Following Topical Application of [^{14}C]-Propiconazole in Spray Dilution 1 (6.25 g/L) to Human Split-Thickness Membranes**

	Cell Number and Donor Number							
Time (h)	Cell 9 (1357)	Cell 10 (1357)	Cell 11 (1382)	*Cell 12 (1382)*	Cell 13 (1368)	Cell 14 (1368)	*Cell 15 (1472)*	Cell 16 (1472)
0	0.00	0.00	0.00	*0.00*	0.00	0.00	*0.00*	0.00
2	0.24	0.24	0.19	*0.19*	0.30	0.78	*0.03*	0.02
4	1.00	1.32	0.73	*0.70*	1.31	2.01	*0.15*	0.19
6	1.83	2.50	1.32	*1.30*	2.28	3.18	*0.33*	0.47
8	2.82	4.19	2.05	*2.09*	3.13	4.28	*0.56*	0.84
12	4.41	6.42	2.99	*3.22*	4.68	5.86	*1.05*	1.48
24	6.88	10.14	4.48	*4.59*	6.74	7.67	*2.12*	2.97

	Cell Number and Donor Number									
Time (h)	Cell 77 (1370)	Cell 78 (1370)	Cell 79 (1445)	Cell 80 (1445)	Cell 81 (1344)	Cell 82 (1344)	Cell 83 (1449)	Cell 84 (1449)	Mean	SD
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2	0.09	0.02	0.06	0.08	0.46	0.18	0.14	0.15	0.21	0.20
4	0.51	0.19	0.60	0.62	2.12	1.12	0.71	0.81	0.94	0.59
6	1.07	0.63	1.57	1.67	5.19	2.73	1.49	1.62	1.97	1.20
8	1.39	1.10	2.57	2.10	5.72	3.78	1.88	2.32	2.73	1.38
12	2.08	1.97	3.89	3.60	8.82	6.18	3.02	3.09	4.18	2.05
24	2.63	4.14	7.12	6.22	12.03	8.72	4.66	4.37	6.34	2.71

Cells 12 and 15 were excluded due to low mass balance

TABLE 12 **Distribution of Radioactivity (µg equiv./cm^2) at 24 h Post Dose Following Topical Application of [^{14}C]-Propiconazole in Spray Dilution 1 (6.25 g/L) to Human Split-Thickness Membranes**

	Cell Number and Donor Number							
	Cell 9 (1357)	Cell 10 (1357)	Cell 11 (1382)	*Cell 12 (1382)*	Cell 13 (1368)	Cell 14 (1368)	*Cell 15 (1472)*	Cell 16 (1472)
Skin Wash 6 h	21.88	15.58	24.83	*16.28*	13.42	22.01	*18.12*	11.54
Tissue Swab 6 h	31.35	34.45	28.67	*31.83*	37.76	27.17	*23.01*	39.03
Pipette Tip 6 h	0.09	0.14	0.03	*0.02*	0.10	0.06	*0.08*	0.14
Skin Wash 24 h	1.85	2.22	1.63	*0.79*	1.82	2.20	*1.32*	2.75
Tissue Swab 24 h	0.83	0.53	0.66	*0.48*	0.67	0.79	*0.78*	0.91
Pipette Tip 24 h	0.00	0.00	0.00	**0.00*	0.00	0.00	*0.00*	0.00
Donor Chamber Wash	0.28	0.04	0.47	*0.70*	0.79	3.20	*0.63*	0.18
Stratum Corneum 1-2	0.14	0.08	0.13	*0.13*	0.12	0.17	*0.07*	0.13
Stratum Corneum 3-5	0.06	0.05	0.06	*0.05*	0.07	0.12	*0.08*	0.13
Stratum Corneum 6-10	0.10	0.08	0.09	*0.05*	0.07	0.07	*0.13*	0.37
Stratum Corneum 11-15	0.06	0.04	0.06	*0.04*	0.04	0.06	*0.09*	0.17
Stratum Corneum 16-20	0.05	0.06	0.07	*0.02*	0.02	0.05	*0.08*	0.24
Unexposed Skin	0.01	0.02	0.01	*0.01*	0.02	0.00	*0.01*	0.02
Exposed Skin	1.38	1.83	0.74	*0.69*	1.44	1.17	*0.78*	1.06
Receptor Fluid	4.47	6.59	2.91	2.98	4.38	4.98	1.38	1.93
Receptor Chamber Wash	0.35	0.40	0.18	*0.18*	0.17	0.39	*0.18*	0.20
Mass Balance	62.92	62.14	60.55	*54.25*	60.89	62.44	*46.73*	58.79

Cells 12 and 15 were excluded due to low mass balance
*=Results calculated from data less than 30 d.p.m. above background

	Cell Number and Donor Number									
	Cell 77 (1370)	Cell 78 (1370)	Cell 79 (1445)	Cell 80 (1445)	Cell 81 (1344)	Cell 82 (1344)	Cell 83 (1449)	Cell 84 (1449)	Mean	SD
Skin Wash 6 h	17.00	17.05	23.04	18.15	23.32	27.73	19.13	26.29	20.07	4.86
Tissue Swab 6 h	30.92	30.82	24.27	27.64	23.18	20.18	32.33	28.69	29.75	5.28
Pipette Tip 6 h	0.01	0.02	0.01	0.07	0.02	0.02	0.06	0.04	0.06	0.05
Skin Wash 24 h	1.64	1.34	0.79	1.21	1.06	0.92	1.43	1.54	1.60	0.54
Tissue Swab 24 h	2.54	2.64	0.43	0.74	1.29	0.30	0.52	0.92	0.98	0.72
Pipette Tip 24 h	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	°0.00	°0.00
Donor Chamber Wash	0.10	0.11	0.09	0.37	0.11	0.10	0.73	0.56	0.51	0.81
Stratum Corneum 1-2	0.14	0.18	0.03	0.02	0.02	0.02	0.10	0.02	0.09	0.06
Stratum Corneum 3-5	0.07	0.14	0.02	0.02	0.02	0.03	0.07	0.04	0.07	0.04
Stratum Corneum 6-10	0.04	0.14	0.02	0.04	0.04	0.05	0.06	0.05	0.09	0.09
Stratum Corneum 11-15	0.02	0.08	0.01	0.04	0.03	0.05	0.06	0.03	0.06	0.04
Stratum Corneum 16-20	0.01	0.06	0.02	0.03	0.02	0.03	0.05	0.04	0.05	0.06
Unexposed Skin	0.01	0.02	0.03	0.02	0.01	0.00	0.01	0.00	0.01	0.01
Exposed Skin	0.15	1.32	1.65	1.80	1.26	0.98	0.74	0.74	1.16	0.47
Receptor Fluid	1.56	2.46	4.23	3.69	7.15	5.18	2.77	2.59	3.92	1.68
Receptor Chamber Wash	0.10	0.18	0.28	0.24	0.95	0.30	0.19	0.46	0.31	0.21
Mass Balance	54.31	56.55	54.93	54.08	58.49	55.90	58.26	62.00	58.73	3.16

°=Mean includes results calculated from data less than 30 d.p.m above background

TABLE 13 **Cumulative Absorption (µg equiv./cm^2) of [^{14}C]-Propiconazole into Receptor Fluid Following Topical Application of [^{14}C]-Propiconazole in Spray Dilution 1 (6.25 g/L) to Human Split-Thickness Membranes**

	Cell number and Donor Number							
Time (h)	Cell 9 (1357)	Cell 10 (1357)	Cell 11 (1382)	*Cell 12 (1382)*	Cell 13 (1368)	Cell 14 (1368)	*Cell 15 (1472)*	Cell 16 (1472)
0	0.00	0.00	0.00	*0.00*	0.00	0.00	*0.00*	0.00
2	0.16	0.16	0.13	*0.13*	0.19	0.51	*0.02*	0.01
4	0.65	0.86	0.48	*0.46*	0.85	1.30	*0.10*	0.12
6	1.19	1.62	0.86	*0.84*	1.48	2.07	*0.22*	0.31
8	1.83	2.72	1.33	*1.36*	2.03	2.78	*0.36*	0.55
12	2.86	4.17	1.95	*2.09*	3.05	3.81	*0.68*	0.96
24	4.47	6.59	2.91	*2.98*	4.38	4.98	*1.38*	1.93

	Cell number and Donor Number									
Time (h)	Cell 77 (1370)	Cell 78 (1370)	Cell 79 (1445)	Cell 80 (1445)	Cell 81 (1344)	Cell 82 (1344)	Cell 83 (1449)	Cell 84 (1449)	Mean	SD
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2	0.06	0.01	0.04	0.05	0.27	0.10	0.08	0.09	0.13	0.13
4	0.30	0.12	0.36	0.37	1.26	0.67	0.42	0.48	0.59	0.37
6	0.64	0.38	0.93	0.99	3.08	1.62	0.89	0.96	1.22	0.73
8	0.82	0.65	1.52	1.25	3.40	2.25	1.12	1.38	1.69	0.86
12	1.23	1.17	2.31	2.14	5.24	3.67	1.80	1.83	2.58	1.27
24	1.56	2.46	4.23	3.69	7.15	5.18	2.77	2.59	3.92	1.68

Cells 12 and 15 were excluded due to low mass balance

TABLE 14 **Distribution of Radioactivity (µg equiv./cm^2) in the *Stratum Corneum* at 24 h Post Dose Following Topical Application of [^{14}C]-Propiconazole in Spray Dilution 1 (6.25 g/L) to Human Split-Thickness Membranes**

	Cell Number and Donor Number							
Tape Strip No.	Cell 9 (1357)	Cell 10 (1357)	Cell 11 (1382)	*Cell 12 (1382)*	Cell 13 (1368)	Cell 14 (1368)	*Cell 15 (1472)*	Cell 16 (1472)
1	0.10	0.05	0.08	*0.09*	0.08	0.08	*0.04*	0.08
2	0.04	0.03	0.05	*0.04*	0.05	0.09	*0.03*	0.04
3	0.03	0.02	0.03	*0.02*	0.03	0.05	*0.04*	0.04
4	0.02	0.02	0.02	*0.02*	0.03	0.02	*0.02*	0.06
5	0.02	0.01	0.02	*0.01*	0.01	0.05	*0.03*	0.04
6	0.01	0.03	0.01	*0.02*	0.01	0.02	*0.02*	0.09
7	0.02	0.02	0.01	*0.01*	0.01	0.02	*0.02*	0.06
8	0.03	0.02	0.01	*0.01*	0.01	0.01	*0.04*	0.07
9	0.02	0.01	0.02	*0.01*	0.02	0.01	*0.03*	0.07
10	0.01	0.01	0.03	*0.01*	0.02	0.01	*0.02*	0.07
11	0.02	0.01	0.01	*0.01*	0.00	0.01	*0.02*	0.05
12	0.01	0.01	0.01	*0.01*	0.01	0.01	*0.02*	0.02
13	0.01	0.01	0.01	*0.01*	0.02	0.02	*0.01*	0.03
14	0.01	0.01	0.01	*0.01*	0.01	0.01	*0.03*	0.03
15	0.01	0.01	0.01	*0.00*	0.00	0.01	*0.02*	0.03
16	0.02	0.01	0.02	*0.00*	0.00	0.01	*0.02*	0.06
17	0.01	0.01	0.01	*0.00*	0.01	0.01	*0.02*	0.06
18	0.01	0.02	0.02	*0.00*	0.00	0.01	*0.02*	0.03
19	0.00	0.02	0.01	*0.00*	0.00	0.01	*0.01*	0.04
20	0.00	0.01	0.01	*0.00*	0.00	0.01	*0.01*	0.05

Cells 12 and 15 were excluded due to low mass balance

Tape Strip No.	Cell Number and Donor Number									
	Cell 77 (1370)	Cell 78 (1370)	Cell 79 (1445)	Cell 80 (1445)	Cell 81 (1344)	Cell 82 (1344)	Cell 83 (1449)	Cell 84 (1449)	Mean	SD
1	0.08	0.10	0.01	0.01	0.01	0.01	0.06	0.01	0.05	0.04
2	0.06	0.08	0.01	0.00	0.01	0.01	0.04	0.01	0.04	0.02
3	0.04	0.06	0.01	0.01	0.01	0.01	0.04	0.02	0.03	0.02
4	0.02	0.04	0.01	0.01	0.01	0.01	0.02	0.01	0.02	0.01
5	0.01	0.04	0.01	0.00	0.01	0.01	0.02	0.01	0.02	0.01
6	0.01	0.04	0.00	0.00	0.01	0.01	E.C.	0.01	0.02	0.02
7	0.01	0.02	0.00	0.01	0.01	0.01	0.02	0.01	0.02	0.01
8	0.01	0.02	0.00	0.01	0.01	0.01	0.01	0.01	0.02	0.02
9	0.01	0.02	0.00	0.01	0.01	0.01	0.01	0.01	0.02	0.02
10	0.01	0.02	0.00	0.01	0.01	0.01	0.01	0.01	0.02	0.02
11	0.01	0.02	0.00	0.01	0.01	0.01	0.02	0.01	0.01	0.01
12	0.01	0.02	0.00	0.01	0.01	0.01	0.01	0.01	0.01	0.01
13	0.00	0.02	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
14	0.00	0.02	0.00	0.01	0.01	0.01	0.01	0.01	0.01	0.01
15	0.00	0.01	0.00	0.00	0.01	0.01	0.01	0.01	0.01	0.01
16	0.00	0.01	0.00	0.00	0.00	0.01	0.01	0.01	0.01	0.02
17	0.00	0.01	0.00	0.01	0.00	0.01	0.01	0.01	0.01	0.01
18	0.00	0.01	0.01	0.01	0.00	0.01	0.01	0.01	0.01	0.01
19	0.00	0.01	0.00	0.01	E.C.	0.01	0.01	0.01	0.01	0.01
20	0.00	0.01	0.00	0.01	0.01	0.01	0.01	0.01	0.01	0.01

E.C. = Epidermal Content

TABLE 15 **Distribution of Radioactivity (% Applied Dose) at 24 h Post Dose Following Topical Application of [^{14}C]-Propiconazole in Spray Dilution 2 (0.625 g/L) to Human Split-Thickness Membranes**

	Cell Number and Donor Number									
	Cell 17 1357	Cell 18 1357	Cell 19 1382	*Cell 20* *1382*	Cell 21 1368	Cell 22 1368	Cell 23 1472	Cell 24 1472	Mean	SD
Skin Wash 6 h	36.31	35.68	21.59	*26.30*	36.98	29.72	37.52	39.95	33.97	6.29
Tissue Swab 6 h	28.97	30.92	33.04	*36.69*	32.84	47.01	29.97	32.60	33.62	6.11
Pipette Tip 6 h	0.28	0.42	0.27	*0.77*	2.65	0.22	0.14	0.60	0.65	0.89
Skin Wash 24 h	6.04	3.31	3.03	*2.81*	3.28	1.34	9.49	3.69	4.31	2.67
Tissue Swab 24 h	2.12	2.17	0.77	*1.06*	2.69	0.52	3.78	2.56	2.09	1.13
Pipette Tip 24 h	0.01	*0.00	0.01	**0.00*	*0.00	*0.00	0.01	*0.00	°0.01	°0.00
Donor Chamber Wash	0.35	0.36	0.86	*0.79*	1.74	2.35	1.15	0.91	1.10	0.73
Stratum Corneum 1-2	0.20	0.08	0.28	*0.18*	0.24	0.04	0.52	0.03	0.20	0.17
Stratum Corneum 3-5	0.27	0.07	0.18	*0.08*	0.12	0.04	0.73	0.03	0.21	0.25
Stratum Corneum 6-10	0.27	0.15	0.16	*0.21*	0.09	0.03	0.97	0.08	0.25	0.32
Stratum Corneum 11-15	0.24	0.13	0.16	*0.14*	0.09	0.04	0.72	0.10	0.21	0.23
Stratum Corneum 16-20	0.23	0.08	0.12	*0.11*	0.05	0.03	0.46	0.12	0.16	0.15
Unexposed Skin	0.03	0.02	0.16	*0.02*	0.05	0.08	0.02	0.04	0.06	0.05
Exposed Skin	7.12	5.30	4.63	*2.26*	1.12	0.90	4.98	3.89	3.99	2.26
Receptor Fluid	11.95	13.13	25.34	*12.82*	15.49	9.90	5.34	11.84	13.28	6.17
Receptor Chamber Wash	0.86	0.79	1.48	*0.97*	0.84	0.55	0.35	0.78	0.81	0.35
Mass Balance	95.24	92.60	92.07	*85.23*	98.28	92.77	96.15	97.24	94.91	2.46

Cell 20 was excluded due to low mass balance
*=Results calculated from data less than 30 d.p.m. above background
°=Mean includes results calculated from data less than 30 d.p.m above background

TABLE 16 **Cumulative Absorption (% Applied Dose) of [^{14}C]-Propiconazole into Receptor Fluid Following Topical Application of the [^{14}C]-Propiconazole in Spray Dilution 2 (0.625 g/L) to Human Split-Thickness Membranes**

	Cell Number and Donor Number									
Time (h)	Cell 17 1357	Cell 18 1357	Cell 19 1382	*Cell 20 1382*	Cell 21 1368	Cell 22 1368	Cell 23 1472	Cell 24 1472	Mean	SD
0	0.00	0.00	0.00	*0.00*	0.00	0.00	0.00	0.00	0.00	0.00
2	0.35	0.23	0.77	*0.41*	3.05	1.19	0.15	0.28	0.86	1.04
4	1.77	1.41	4.16	*2.26*	7.18	3.01	0.56	1.72	2.83	2.25
6	3.43	3.22	8.96	*4.23*	10.04	4.63	1.47	3.57	5.04	3.20
8	4.99	5.11	12.82	*6.41*	12.21	6.52	2.38	5.88	7.13	3.90
12	7.85	8.06	17.30	*9.06*	14.15	8.14	3.46	8.48	9.63	4.59
24	11.95	13.13	25.34	*12.82*	15.49	9.90	5.34	11.84	13.28	6.17

Cell 20 was excluded due to low mass balance

TABLE 17 Distribution of Radioactivity (µg equiv./cm^2) at 24 h Post Dose Following Topical Application of [^{14}C]-Propiconazole in Spray Dilution 2 (0.625 g/L) to Human Split-Thickness Membranes

	Cell Number and Donor Number									
	Cell 17 1357	Cell 18 1357	Cell 19 1382	*Cell 20* *1382*	Cell 21 1368	Cell 22 1368	Cell 23 1472	Cell 24 1472	Mean	SD
Skin Wash 6 h	2.41	2.37	1.43	*1.75*	2.46	1.97	2.49	2.65	2.26	0.42
Tissue Swab 6 h	1.92	2.05	2.20	*2.44*	2.18	3.12	1.99	2.17	2.23	0.41
Pipette Tip 6 h	0.02	0.03	0.02	*0.05*	0.18	0.01	0.01	0.04	0.04	0.06
Skin Wash 24 h	0.40	0.22	0.20	*0.19*	0.22	0.09	0.63	0.24	0.29	0.18
Tissue Swab 24 h	0.14	0.14	0.05	*0.07*	0.18	0.03	0.25	0.17	0.14	0.08
Pipette Tip 24 h	0.00	*0.00	0.00	**0.00*	*0.00	*0.00	0.00	*0.00	°0.00	°0.00
Donor Chamber Wash	0.02	0.02	0.06	*0.05*	0.12	0.16	0.08	0.06	0.07	0.05
Stratum Corneum 1-2	0.01	0.01	0.02	*0.01*	0.02	0.00	0.03	0.00	0.01	0.01
Stratum Corneum 3-5	0.02	0.00	0.01	*0.01*	0.01	0.00	0.05	0.00	0.01	0.02
Stratum Corneum 6-10	0.02	0.01	0.01	*0.01*	0.01	0.00	0.06	0.01	0.02	0.02
Stratum Corneum 11-15	0.02	0.01	0.01	*0.01*	0.01	0.00	0.05	0.01	0.01	0.02
Stratum Corneum 16-20	0.02	0.01	0.01	*0.01*	0.00	0.00	0.03	0.01	0.01	0.01
Unexposed Skin	0.00	0.00	0.01	*0.00*	0.00	0.01	0.00	0.00	0.00	0.00
Exposed Skin	0.47	0.35	0.31	*0.15*	0.07	0.06	0.33	0.26	0.27	0.15
Receptor Fluid	0.79	0.87	1.68	*0.85*	1.03	0.66	0.35	0.79	0.88	0.41
Receptor Chamber Wash	0.06	0.05	0.10	*0.06*	0.06	0.04	0.02	0.05	0.05	0.02
Mass Balance	6.33	6.15	6.12	*5.66*	6.53	6.16	6.39	6.46	6.31	0.16

Cell 20 was excluded due to low mass balance
*=Results calculated from data less than 30 d.p.m. above background
°=Mean includes results calculated from data less than 30 d.p.m above background

TABLE 18 **Cumulative Absorption (µg equiv./cm^2) of [^{14}C]-Propiconazole into Receptor Fluid Following Topical Application of [^{14}C]-Propiconazole in Spray Dilution 2 (0.625 g/L) to Human Split-Thickness Membranes**

	Cell Number and Donor Number									
Time (h)	Cell 17 1357	Cell 18 1357	Cell 19 1382	*Cell 20 1382*	Cell 21 1368	Cell 22 1368	Cell 23 1472	Cell 24 1472	Mean	SD
0	0.00	0.00	0.00	*0.00*	0.00	0.00	0.00	0.00	0.00	0.00
2	0.02	0.02	0.05	*0.03*	0.20	0.08	0.01	0.02	0.06	0.07
4	0.12	0.09	0.28	*0.15*	0.48	0.20	0.04	0.11	0.19	0.15
6	0.23	0.21	0.60	*0.28*	0.67	0.31	0.10	0.24	0.34	0.21
8	0.33	0.34	0.85	*0.43*	0.81	0.43	0.16	0.39	0.47	0.26
12	0.52	0.54	1.15	*0.60*	0.94	0.54	0.23	0.56	0.64	0.30
24	0.79	0.87	1.68	*0.85*	1.03	0.66	0.35	0.79	0.88	0.41

Cell 20 was excluded due to low mass balance

TABLE 19 **Distribution of Radioactivity (µg equiv./cm^2) in the *Stratum Corneum* at 24 h Post Dose Following Topical Application of [^{14}C]-Propiconazole in Spray Dilution 2 (0.625 g/L) to Human Split-Thickness Membranes**

	Cell Number and Donor Number									
Tape Strip No.	Cell 17 1357	Cell 18 1357	Cell 19 1382	*Cell 20 1382*	Cell 21 1368	Cell 22 1368	Cell 23 1472	Cell 24 1472	Mean	SD
1	0.008	0.004	0.013	*0.009*	0.011	0.002	0.015	0.001	0.008	0.005
2	0.006	0.002	0.005	*0.003*	0.005	0.001	0.019	0.001	0.006	0.006
3	0.006	0.002	0.003	*0.002*	0.003	0.001	0.015	0.001	0.004	0.005
4	0.006	0.002	0.005	*0.002*	0.004	0.001	0.014	0.001	0.005	0.004
5	0.006	0.001	0.004	*0.002*	0.002	0.001	0.020	0.001	0.005	0.007
6	0.005	0.002	0.003	*0.003*	0.002	*0.000	0.014	0.001	°0.004	°0.005
7	0.004	0.003	0.002	*0.003*	0.001	0.000	0.012	0.001	0.003	0.004
8	0.006	0.002	0.002	*0.002*	0.001	0.001	0.011	0.002	0.003	0.004
9	0.003	0.001	0.002	*0.003*	0.001	0.001	0.010	0.001	0.003	0.003
10	0.001	0.001	0.002	*0.003*	0.001	*0.000	0.018	0.001	°0.004	°0.006
11	0.003	0.002	0.003	*0.002*	0.002	0.001	0.007	0.001	0.003	0.002
12	0.003	0.002	0.002	*0.002*	0.001	0.000	0.013	0.001	0.003	0.004
13	0.003	0.002	0.002	*0.002*	0.001	0.001	0.006	0.002	0.002	0.002
14	0.003	0.001	0.003	*0.002*	0.001	0.000	0.017	0.001	0.004	0.006
15	0.004	0.001	0.001	*0.002*	0.001	0.000	0.005	0.001	0.002	0.002
16	0.003	0.002	0.001	*0.001*	0.001	*0.000	0.007	0.001	°0.002	°0.002
17	0.004	0.001	0.003	*0.001*	0.001	0.000	0.007	0.002	0.003	0.002
18	0.003	0.001	0.002	*0.001*	0.001	0.000	0.005	0.002	0.002	0.002
19	0.003	0.001	0.002	*0.002*	0.000	0.000	0.006	0.001	0.002	0.002
20	0.001	0.001	0.001	*0.001*	0.001	0.000	0.007	0.002	0.002	0.002

Cell 20 was excluded due to low mass balance
E.C. = Epidermal Content
*=Results calculated from data less than 30 d.p.m. above background
°=Mean includes results calculated from data less than 30 d.p.m above background

TABLE 20 **Distribution of Radioactivity (% Applied Dose) at 24 h Post Dose Following Topical Application of [^{14}C]-Fenpropidin in Formulation Concentrate (275 g/L) to Human Split-Thickness Membranes**

	Cell Number and Donor Number							
	Cell 25 (1362)	Cell 26 (1362)	*Cell 27 (1418)*	Cell 28 (1418)	Cell 29 (1371)	Cell 30 (1371)	Cell 31 (1347)	*Cell 32 (1347)*
Skin Wash 6 h	25.65	36.74	*59.56*	31.94	36.15	59.80	36.57	*42.18*
Tissue Swab 6 h	67.22	50.48	*11.59*	60.10	55.72	24.83	56.84	*33.48*
Pipette Tip 6 h	0.20	1.45	*0.02*	0.10	0.45	0.02	0.06	*0.76*
Skin Wash 24 h	0.52	0.54	*0.28*	0.57	0.39	4.18	0.40	*0.59*
Tissue Swab 24 h	0.17	0.53	*0.16*	0.34	0.13	1.21	0.13	*0.14*
Pipette Tip 24 h	0.01	0.04	*0.01*	0.01	*0.00	0.01	0.01	*0.00*
Donor Chamber Wash	0.31	0.12	*0.06*	0.15	0.06	0.72	0.09	*0.12*
Stratum Corneum 1-2	0.02	0.04	*0.02*	0.10	0.02	0.87	0.03	*0.05*
Stratum Corneum 3-5	0.02	0.03	*0.01*	0.04	0.01	0.26	0.03	*0.02*
Stratum Corneum 6-10	0.05	0.04	*0.00*	0.04	0.01	0.06	0.04	*0.02*
Stratum Corneum 11-15	0.03	0.02	*0.01*	0.02	0.01	0.04	0.02	*0.01*
Stratum Corneum 16-20	0.01	0.01	*0.01*	0.01	0.01	0.05	0.01	*0.01*
Unexposed Skin	0.02	0.02	*0.00*	0.00	*0.00	0.03	0.01	*0.01*
Exposed Skin	0.86	0.61	*0.20*	0.27	0.15	0.81	0.27	*0.18*
Receptor Fluid	0.75	0.58	*0.46*	0.52	0.59	2.04	1.43	*0.57*
Receptor Chamber Wash	0.07	0.07	*0.03*	0.04	0.03	0.18	0.10	**0.04*
Mass Balance	95.91	91.31	*72.41*	94.25	93.75	95.09	96.06	*78.20*

Cells 27 and 32 were excluded due to low mass balance
*=Results calculated from data less than 30 d.p.m. above background

	Cell Number and Donor Number									
	Cell 61 (1370)	Cell 62 (1370)	Cell 63 (1445)	Cell 64 (1445)	Cell 65 (1344)	Cell 66 (1344)	Cell 67 (1449)	Cell 68 (1449)	Mean	SD
Skin Wash 6 h	39.72	27.85	19.44	32.63	28.14	21.24	46.08	45.62	34.83	10.78
Tissue Swab 6 h	52.93	59.73	80.74	60.27	64.27	74.27	47.19	50.86	57.53	13.22
Pipette Tip 6 h	0.03	0.07	0.06	0.03	0.05	0.10	0.02	0.10	0.19	0.38
Skin Wash 24 h	0.36	0.95	0.39	0.30	0.66	0.50	0.17	0.42	0.74	1.01
Tissue Swab 24 h	0.17	1.50	0.46	0.11	0.47	0.28	0.09	0.25	0.42	0.42
Pipette Tip 24 h	*0.00	0.01	*0.00	*0.00	*0.00	0.00	*0.00	0.00	°0.01	°0.01
Donor Chamber Wash	0.07	0.35	0.10	0.09	0.06	0.08	0.25	0.25	0.19	0.18
Stratum Corneum 1-2	0.16	0.26	0.01	0.01	0.04	0.02	0.03	0.08	0.12	0.23
Stratum Corneum 3-5	0.11	0.14	0.01	0.01	0.03	0.04	0.03	0.06	0.06	0.07
Stratum Corneum 6-10	0.04	0.10	0.02	0.02	0.03	0.05	0.03	0.04	0.04	0.02
Stratum Corneum 11-15	0.01	0.04	0.02	0.01	0.01	0.03	0.02	0.01	0.02	0.01
Stratum Corneum 16-20	0.01	0.03	0.02	0.01	0.01	0.01	0.01	0.00	0.01	0.01
Unexposed Skin	0.00	0.00	0.01	0.02	0.00	0.00	0.00	0.01	°0.01	°0.01
Exposed Skin	0.17	0.43	1.03	1.19	0.21	0.26	0.11	0.22	0.47	0.36
Receptor Fluid	0.54	1.01	1.30	0.94	1.50	1.91	0.42	0.82	1.02	0.53
Receptor Chamber Wash	0.03	0.07	0.08	0.08	0.09	0.16	0.03	0.05	°0.08	°0.05
Mass Balance	94.35	92.53	103.67	95.71	95.55	98.96	94.48	98.78	95.74	3.07

*=Results calculated from data less than 30 d.p.m. above background
°=Mean includes results calculated from data less than 30 d.p.m above background

TABLE 21 **Cumulative Absorption (% Applied Dose) of [^{14}C]-Fenpropidin into Receptor Fluid Following Topical Application of the [^{14}C]-Fenpropidin in Formulation Concentrate (275 g/L) to Human Split-Thickness Membranes**

	Cell Number and Donor Number							
Time (h)	Cell 25 (1362)	Cell 26 (1362)	*Cell 27 (1418)*	Cell 28 (1418)	Cell 29 (1371)	Cell 30 (1371)	Cell 31 (1347)	*Cell 32 (1347)*
0	0.00	0.00	*0.00*	0.00	0.00	0.00	0.00	*0.00*
2	*0.00	*0.00	**0.00*	*0.00	*0.00	*0.01	0.03	**0.00*
4	*0.02	*0.01	*0.03*	*0.01	0.02	0.06	0.18	**0.02*
6	0.07	0.03	*0.09*	0.04	0.09	0.18	0.41	*0.07*
8	0.12	0.07	*0.17*	0.08	0.18	0.42	0.73	*0.13*
12	0.26	0.19	*0.33*	0.21	0.36	0.83	1.16	*0.30*
24	0.75	0.58	*0.46*	0.52	0.59	2.04	1.43	*0.57*

	Cell Number and Donor Number									
Time (h)	Cell 61 (1370)	Cell 62 (1370)	Cell 63 (1445)	Cell 64 (1445)	Cell 65 (1344)	Cell 66 (1344)	Cell 67 (1449)	Cell 68 (1449)	Mean	SD
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2	*0.01	*0.01	*0.00	*0.00	*0.01	*0.01	*0.00	0.02	°0.01	°0.01
4	0.03	0.04	0.02	*0.02	0.11	0.09	*0.02	0.10	°0.05	°0.05
6	0.11	0.15	0.10	0.11	0.40	0.37	0.07	0.27	0.17	0.14
8	0.18	0.24	0.21	0.22	0.56	0.58	0.14	0.38	0.29	0.21
12	0.35	0.50	0.52	0.50	1.01	1.16	0.29	0.58	0.57	0.34
24	0.54	1.01	1.30	0.94	1.50	1.91	0.42	0.82	1.02	0.53

Cells 27 and 32 were excluded due to low mass balance
*=Results calculated from data less than 30 d.p.m. above background
°=Mean includes results calculated from data less than 30 d.p.m above background

TABLE 22 **Distribution of Radioactivity (µg equiv./cm^2) at 24 h Post Dose Following Topical Application of [^{14}C]-Fenpropidin in Formulation Concentrate (275 g/L) to Human Split-Thickness Membranes**

	Cell Number and Donor Number							
	Cell 25 (1362)	Cell 26 (1362)	*Cell 27 (1418)*	Cell 28 (1418)	Cell 29 (1371)	Cell 30 (1371)	Cell 31 (1347)	*Cell 32 (1347)*
Skin Wash 6 h	705.01	1009.90	*1637.12*	877.94	993.62	1643.85	1005.11	*1159.57*
Tissue Swab 6 h	1847.79	1387.63	*318.45*	1651.92	1531.73	682.47	1562.35	*920.42*
Pipette Tip 6 h	5.51	39.98	*0.67*	2.63	12.36	0.41	1.56	*21.01*
Skin Wash 24 h	14.33	14.78	*7.61*	15.58	10.85	114.82	11.09	*16.22*
Tissue Swab 24 h	4.72	14.46	*4.32*	9.42	3.68	33.35	3.67	*3.87*
Pipette Tip 24 h	0.31	1.15	*0.24*	0.41	*0.03	0.35	0.41	*0.05*
Donor Chamber Wash	8.63	3.25	*1.56*	4.00	1.76	19.71	2.58	*3.32*
Stratum Corneum 1-2	0.49	1.12	*0.53*	2.74	0.63	23.80	0.76	*1.35*
Stratum Corneum 3-5	0.64	0.72	*0.23*	1.06	0.34	7.03	0.93	*0.53*
Stratum Corneum 6-10	1.36	1.16	*0.13*	1.06	0.38	1.68	0.97	*0.60*
Stratum Corneum 11-15	0.71	0.46	*0.19*	0.65	0.18	0.97	0.64	*0.27*
Stratum Corneum 16-20	0.32	0.35	*0.21*	0.34	0.16	1.30	0.26	*0.20*
Unexposed Skin	0.48	0.43	*0.14*	0.09	*0.03	0.90	0.37	*0.18*
Exposed Skin	23.52	16.70	*5.36*	7.38	4.25	22.24	7.46	*5.08*
Receptor Fluid	20.60	15.91	*12.63*	14.36	16.18	55.95	39.41	*15.63*
Receptor Chamber Wash	1.93	1.81	*0.96*	1.08	0.90	5.06	2.84	**1.21*
Mass Balance	2636.36	2509.82	*1990.34*	2590.67	2577.10	2613.91	2640.39	*2149.51*

Cells 27 and 32 were excluded due to low mass balance
*=Results calculated from data less than 30 d.p.m. above background

	Cell Number and Donor Number									
	Cell 61 (1370)	Cell 62 (1370)	Cell 63 (1445)	Cell 64 (1445)	Cell 65 (1344)	Cell 66 (1344)	Cell 67 (1449)	Cell 68 (1449)	Mean	SD
Skin Wash 6 h	1091.58	765.39	534.25	896.80	773.48	583.71	1266.36	1253.78	957.20	296.38
Tissue Swab 6 h	1454.72	1641.69	2219.05	1656.39	1766.24	2041.29	1297.07	1397.84	1581.30	363.37
Pipette Tip 6 h	0.74	2.01	1.64	0.72	1.33	2.77	0.50	2.79	5.36	10.43
Skin Wash 24 h	9.81	26.05	10.58	8.13	18.09	13.66	4.78	11.43	20.29	27.67
Tissue Swab 24 h	4.71	41.10	12.59	3.14	12.78	7.76	2.36	6.94	11.48	11.68
Pipette Tip 24 h	*0.02	0.14	*0.03	*0.00	*0.02	0.11	*0.00	0.09	°0.22	°0.31
Donor Chamber Wash	1.82	9.64	2.77	2.60	1.51	2.22	7.01	6.93	5.32	4.95
Stratum Corneum 1-2	4.36	7.15	0.30	0.20	1.01	0.65	0.70	2.09	3.29	6.21
Stratum Corneum 3-5	3.15	3.74	0.35	0.28	0.92	1.16	0.69	1.53	1.61	1.87
Stratum Corneum 6-10	1.14	2.88	0.58	0.44	0.78	1.26	0.94	0.97	1.11	0.62
Stratum Corneum 11-15	0.32	1.03	0.50	0.32	0.29	0.76	0.49	0.22	0.54	0.27
Stratum Corneum 16-20	0.19	0.71	0.41	0.29	0.15	0.32	0.17	0.12	0.36	0.31
Unexposed Skin	0.04	0.10	0.23	0.46	0.05	0.10	0.05	0.18	0.25	0.25
Exposed Skin	4.76	11.82	28.18	32.70	5.70	7.11	3.06	5.99	12.92	9.89
Receptor Fluid	14.74	27.74	35.63	25.81	41.17	52.60	11.65	22.61	28.17	14.55
Receptor Chamber Wash	0.88	1.86	2.12	2.08	2.55	4.27	0.72	1.37	2.11	1.26
Mass Balance	2592.99	2543.06	2849.22	2630.38	2626.07	2719.73	2596.55	2714.87	2631.51	84.37

*=Results calculated from data less than 30 d.p.m. above background
°=Mean includes results calculated from data less than 30 d.p.m above background

TABLE 23 **Cumulative Absorption (µg equiv./cm^2) of [^{14}C]-Fenpropidin into Receptor Fluid Following Topical Application of [^{14}C]-Fenpropidin in Formulation Concentrate (275 g/L) to Human Split-Thickness Membranes**

	Cell Number and Donor Number							
Time (h)	Cell 25 (1362)	Cell 26 (1362)	*Cell 27 (1418)*	Cell 28 (1418)	Cell 29 (1371)	Cell 30 (1371)	Cell 31 (1347)	*Cell 32 (1347)*
0	0.00	0.00	*0.00*	0.00	0.00	0.00	0.00	*0.00*
2	*0.08	*0.00	**0.00*	*0.00	*0.00	*0.15	0.78	**0.00*
4	*0.52	*0.25	*0.77*	*0.25	0.67	1.66	4.87	**0.51*
6	1.80	0.82	*2.49*	1.15	2.41	4.99	11.28	*1.89*
8	3.39	2.04	*4.73*	2.28	4.94	11.58	20.02	*3.53*
12	7.19	5.21	*9.17*	5.69	10.03	22.84	31.96	*8.14*
24	20.60	15.91	*12.63*	14.36	16.18	55.95	39.41	*15.63*

	Cell Number and Donor Number									
Time (h)	Cell 61 (1370)	Cell 62 (1370)	Cell 63 (1445)	Cell 64 (1445)	Cell 65 (1344)	Cell 66 (1344)	Cell 67 (1449)	Cell 68 (1449)	Mean	SD
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2	*0.22	*0.18	*0.09	*0.01	*0.38	*0.23	*0.09	0.64	°0.20	°0.24
4	0.93	1.02	0.66	*0.48	3.01	2.46	*0.42	2.63	°1.42	°1.36
6	3.02	4.18	2.80	3.12	11.11	10.17	1.94	7.36	4.72	3.72
8	4.92	6.57	5.74	6.18	15.50	15.86	3.93	10.32	8.09	5.66
12	9.71	13.75	14.20	13.77	27.69	31.97	7.88	15.83	15.55	9.39
24	14.74	27.74	35.63	25.81	41.17	52.60	11.65	22.61	28.17	14.55

Cells 27 and 32 were excluded due to low mass balance
*=Results calculated from data less than 30 d.p.m. above background
°=Mean includes results calculated from data less than 30 d.p.m above background

TABLE 24 **Distribution of Radioactivity (µg equiv./cm^2) in the *Stratum Corneum* at 24 h Post Dose Following Topical Application of [^{14}C]-Fenpropidin in Formulation Concentrate (275 g/L) to Human Split-Thickness Membranes**

	Cell Number and Donor Number							
Tape Strip No.	Cell 25 (1362)	Cell 26 (1362)	*Cell 27 (1418)*	Cell 28 (1418)	Cell 29 (1371)	Cell 30 (1371)	Cell 31 (1347)	*Cell 32 (1347)*
1	0.29	0.74	*0.36*	2.03	0.38	16.90	0.44	*1.09*
2	0.20	0.38	*0.17*	0.71	0.25	6.91	0.32	*0.26*
3	0.32	0.21	*0.10*	0.36	0.11	3.46	0.56	*0.19*
4	0.16	0.09	*0.05*	0.44	0.09	2.25	0.15	*0.15*
5	0.17	0.42	*0.09*	0.27	0.14	1.33	0.22	*0.19*
6	0.25	0.63	*0.04*	0.37	0.11	E.C.	0.23	*0.14*
7	0.27	0.18	**0.03*	0.35	0.08	0.39	0.28	*0.09*
8	0.14	0.08	*0.04*	0.17	0.06	0.43	0.17	*0.13*
9	0.48	0.08	**0.03*	0.08	0.05	0.41	0.13	*0.08*
10	0.23	0.19	*E.C.*	0.08	0.07	0.46	0.16	*0.16*
11	0.19	0.13	*0.07*	0.16	0.04	0.21	0.14	*0.07*
12	0.13	0.10	*0.06*	0.10	0.05	0.21	0.13	*0.05*
13	0.19	0.08	*E.C.*	0.15	*0.03	0.19	0.16	*0.09*
14	0.10	0.09	*E.C.*	0.09	0.04	0.22	0.13	**0.02*
15	0.11	0.08	*0.06*	0.15	*0.02	0.14	0.08	*0.04*
16	0.06	0.13	*0.04*	0.10	*0.02	0.41	0.08	*0.08*
17	0.07	0.05	*0.04*	0.06	*0.01	0.21	0.06	*0.04*
18	0.05	0.05	*0.07*	0.10	E.C.	0.22	0.03	*0.04*
19	0.08	0.06	*0.04*	0.04	0.08	0.21	0.03	*0.03*
20	0.05	0.06	**0.03*	0.05	0.04	0.25	0.05	**0.02*

Cells 27 and 32 were excluded due to low mass balance

Tape Strip No.	Cell Number and Donor Number									
	Cell 61 (1370)	Cell 62 (1370)	Cell 63 (1445)	Cell 64 (1445)	Cell 65 (1344)	Cell 66 (1344)	Cell 67 (1449)	Cell 68 (1449)	Mean	SD
1	2.45	4.97	0.15	0.10	0.62	0.29	0.42	1.11	2.21	4.43
2	1.91	2.18	0.15	0.10	0.39	0.36	0.28	0.98	1.08	1.80
3	1.66	1.72	0.17	0.13	0.34	0.39	0.30	0.71	0.74	0.94
4	0.98	1.22	0.09	0.09	0.35	0.40	0.22	0.49	0.50	0.61
5	0.51	0.80	0.10	0.07	0.22	0.37	0.18	0.32	0.36	0.34
6	0.42	0.83	0.13	0.07	0.19	0.25	0.18	0.33	0.31	0.22
7	0.30	0.63	0.10	0.09	0.25	0.30	0.22	0.26	°0.26	°0.14
8	0.17	0.55	0.12	0.11	0.13	0.29	0.19	0.15	0.20	0.14
9	0.12	0.47	0.10	0.10	0.11	0.23	0.17	0.11	°0.19	°0.15
10	0.12	0.40	0.13	0.07	0.12	0.19	0.18	0.12	0.18	0.12
11	0.08	0.25	0.12	0.07	0.07	0.18	0.12	0.07	0.13	0.06
12	0.07	0.24	0.10	0.07	0.06	0.16	0.13	0.05	0.11	0.06
13	0.06	0.21	0.10	0.07	0.05	0.15	0.10	0.05	°0.11	°0.06
14	0.05	0.16	0.09	0.06	0.05	0.12	0.09	*0.03	°0.09	°0.05
15	0.06	0.18	0.09	0.06	0.06	0.15	0.06	*0.03	°0.09	°0.05
16	0.04	0.13	0.10	0.06	*0.03	0.08	*0.03	*0.03	°0.09	°0.10
17	0.04	0.14	0.05	0.05	0.04	0.06	0.05	*0.02	°0.06	°0.05
18	0.04	0.09	0.07	0.06	*0.03	E.C.	*0.02	*0.02	°0.07	°0.05
19	*0.03	0.17	0.09	0.06	E.C.	0.10	0.04	*0.03	°0.08	°0.06
20	0.03	0.17	0.10	0.06	0.05	0.07	*0.03	*0.02	°0.07	°0.06

E.C. = Epidermal Content
*=Results calculated from data less than 30 d.p.m. above background
°=Mean includes results calculated from data less than 30 d.p.m above background

TABLE 25 Distribution of Radioactivity (% Applied Dose) at 24 h Post Dose Following Topical Application of [^{14}C]-Fenpropidin in Spray Dilution 1 (13.75 g/L) to Human Split-Thickness Membranes

	Cell Number and Donor Number									
	Cell 33 1362	Cell 34 1362	Cell 35 1418	Cell 36 1418	Cell 37 1371	Cell 38 1371	Cell 39 1347	Cell 40 1347	Mean	SD
Skin Wash 6 h	31.01	33.12	24.13	42.60	41.31	31.15	34.34	31.80	33.68	5.94
Tissue Swab 6 h	58.25	46.78	45.42	35.99	38.29	44.98	45.13	54.04	46.11	7.34
Pipette Tip 6 h	0.01	0.14	0.10	0.04	0.07	0.30	0.01	0.06	0.09	0.09
Filters 6 h	0.32	0.40	0.29	0.28	0.35	0.31	0.16	0.45	0.32	0.09
Skin Wash 24 h	1.57	3.04	2.51	2.13	2.85	1.60	1.16	1.77	2.08	0.67
Tissue Swab 24 h	0.63	1.42	1.55	1.65	0.85	0.63	0.45	0.61	0.97	0.48
Pipette Tip 24 h	0.01	0.01	0.00	0.01	0.01	0.03	0.02	0.02	0.01	0.01
Donor Chamber Wash/Trap	0.13	0.43	0.32	0.40	0.49	1.06	1.09	0.23	0.52	0.36
Filters 24 h	0.29	0.57	0.31	0.21	0.42	0.17	0.09	0.10	0.27	0.16
Stratum Corneum 1-2	0.11	0.32	0.24	0.18	0.07	0.07	0.36	0.14	0.19	0.11
Stratum Corneum 3-5	0.06	0.20	0.21	0.10	0.08	0.10	0.32	0.06	0.14	0.09
Stratum Corneum 6-10	0.04	0.17	0.08	0.10	0.08	0.10	0.24	0.05	0.11	0.07
Stratum Corneum 11-15	0.04	0.09	0.07	0.08	0.04	0.04	0.19	0.05	0.07	0.05
Stratum Corneum 16-20	0.03	0.05	0.05	0.03	0.01	0.02	0.22	0.04	0.06	0.07
Exposed Skin	1.29	4.28	3.83	1.87	0.57	2.11	4.18	1.71	2.48	1.42
Receptor Fluid	2.87	5.23	18.03	8.64	6.09	5.41	5.48	2.90	6.83	4.88
Receptor Chamber Wash	0.12	0.57	0.83	0.46	0.21	0.55	0.43	0.38	0.44	0.22
Mass Balance	96.81	97.37	98.18	94.85	91.81	90.38	97.22	94.44	95.13	2.82

TABLE 26 **Cumulative Absorption (% Applied Dose) of [^{14}C]-Fenpropidin into Receptor Fluid Following Topical Application of [^{14}C]-Fenpropidin in Spray Dilution 1 (13.75 g/L) to Human Split-Thickness Membranes**

	Cell Number and Donor Number									
Time (h)	Cell 33 1362	Cell 34 1362	Cell 35 1418	Cell 36 1418	Cell 37 1371	Cell 38 1371	Cell 39 1347	Cell 40 1347	Mean	SD
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2	0.06	*0.02	0.13	0.10	0.41	0.14	0.09	0.05	°0.12	°0.12
4	0.77	0.30	1.79	0.90	1.46	0.82	0.61	0.79	0.93	0.48
6	1.29	0.80	4.69	2.22	2.87	1.87	1.41	1.44	2.07	1.23
8	1.97	1.70	7.45	3.94	4.15	2.99	2.34	2.57	3.39	1.86
12	2.33	2.93	11.68	6.00	5.40	4.21	3.52	3.08	4.89	3.01
24	2.87	5.23	18.03	8.64	6.09	5.41	5.48	2.90	6.83	4.88

*=Results calculated from data less than 30 d.p.m. above background
°=Mean includes results calculated from data less than 30 d.p.m above background

TABLE 27 **Distribution of Radioactivity (µg equiv./cm^2) at 24 h Post Dose Following Topical Application of [^{14}C]-Fenpropidin in Spray Dilution 1 (13.75 g/L) to Human Split-Thickness Membranes**

	Cell Number and Donor Number									
	Cell 33 1362	Cell 34 1362	Cell 35 1418	Cell 36 1418	Cell 37 1371	Cell 38 1371	Cell 39 1347	Cell 40 1347	Mean	SD
Skin Wash 6 h	45.66	48.75	35.53	62.71	60.81	45.86	50.56	46.82	49.59	8.74
Tissue Swab 6 h	85.76	68.87	66.86	52.99	56.36	66.21	66.44	79.55	67.88	10.80
Pipette Tip 6 h	0.02	0.21	0.14	0.06	0.10	0.44	0.02	0.08	0.13	0.14
Filters 6 h	0.47	0.58	0.42	0.41	0.51	0.46	0.24	0.67	0.47	0.13
Skin Wash 24 h	2.31	4.47	3.70	3.14	4.20	2.35	1.71	2.61	3.06	0.99
Tissue Swab 24 h	0.92	2.09	2.28	2.42	1.25	0.93	0.66	0.91	1.43	0.71
Pipette Tip 24 h	0.01	0.02	0.00	0.01	0.01	0.05	0.03	0.03	0.02	0.01
Donor Chamber Wash/Trap	0.19	0.64	0.46	0.59	0.72	1.56	1.61	0.34	0.76	0.53
Filters 24 h	0.42	0.84	0.46	0.31	0.61	0.25	0.14	0.15	0.40	0.24
Stratum Corneum 1-2	0.16	0.48	0.35	0.27	0.11	0.10	0.54	0.20	0.28	0.16
Stratum Corneum 3-5	0.08	0.30	0.30	0.15	0.12	0.15	0.47	0.08	0.21	0.14
Stratum Corneum 6-10	0.06	0.24	0.12	0.14	0.12	0.15	0.35	0.08	0.16	0.10
Stratum Corneum 11-15	0.05	0.13	0.10	0.11	0.06	0.05	0.28	0.08	0.11	0.07
Stratum Corneum 16-20	0.04	0.07	0.07	0.05	0.02	0.03	0.33	0.05	0.08	0.10
Unexposed Skin	0.07	0.82	0.30	0.13	0.04	2.57	4.90	0.03	1.11	1.76
Exposed Skin	1.90	6.31	5.64	2.76	0.83	3.11	6.16	2.51	3.65	2.09
Receptor Fluid	4.23	7.69	26.55	12.71	8.96	7.97	8.07	4.27	10.06	7.19
Receptor Chamber Wash	0.18	0.84	1.23	0.68	0.31	0.81	0.63	0.56	0.65	0.33
Mass Balance	142.52	143.35	144.53	139.63	135.15	133.05	143.12	139.03	140.05	4.15

TABLE 28 **Cumulative Absorption (µg equiv./cm^2) of [^{14}C]-Fenpropidin into Receptor Fluid Following Topical Application of [^{14}C]-Fenpropidin in Spray Dilution 1 (13.75 g/L) to Human Split-Thickness Membranes**

	Cell Number and Donor Number									
	Cell 33	Cell 34	Cell 35	Cell 36	Cell 37	Cell 38	Cell 39	Cell 40		
Time (h)	1362	1362	1418	1418	1371	1371	1347	1347	Mean	SD
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2	0.08	*0.03	0.19	0.15	0.61	0.21	0.13	0.07	°0.18	°0.18
4	1.13	0.44	2.64	1.32	2.15	1.21	0.89	1.16	1.37	0.70
6	1.90	1.18	6.91	3.26	4.23	2.76	2.08	2.11	3.05	1.82
8	2.91	2.50	10.97	5.80	6.11	4.41	3.45	3.78	4.99	2.74
12	3.43	4.31	17.19	8.83	7.95	6.19	5.18	4.54	7.20	4.44
24	4.23	7.69	26.55	12.71	8.96	7.97	8.07	4.27	10.06	7.19

*=Results calculated from data less than 30 d.p.m. above background
°=Mean includes results calculated from data less than 30 d.p.m above background

TABLE 29 **Distribution of Radioactivity (µg equiv./cm^2) in the *Stratum Corneum* at 24 h Post Dose Following Topical Application of [^{14}C]-Fenpropidin in Spray Dilution 1 (13.75 g/L) to Human Split-Thickness Membranes**

	Cell Number and Donor Number									
Tape Strip No.	Cell 33 1362	Cell 34 1362	Cell 35 1418	Cell 36 1418	Cell 37 1371	Cell 38 1371	Cell 39 1347	Cell 40 1347	Mean	SD
1	0.11	0.37	0.20	0.17	0.08	E.C.	0.43	0.14	0.21	0.13
2	0.06	0.10	0.16	0.10	0.03	0.10	0.11	0.06	0.09	0.04
3	0.04	0.10	0.15	0.05	0.05	0.08	0.29	0.03	0.10	0.08
4	0.02	0.14	0.08	0.05	0.03	0.04	0.17	0.03	0.07	0.06
5	0.02	0.05	0.07	0.05	0.04	0.03	0.02	0.02	0.04	0.02
6	0.01	0.03	E.C.	0.03	0.04	0.02	0.06	0.03	0.03	0.02
7	0.00	0.08	0.04	0.03	0.03	0.03	0.07	0.02	0.04	0.03
8	0.01	0.04	0.04	0.04	0.02	0.03	0.08	0.02	0.03	0.02
9	0.01	0.05	0.02	0.02	0.02	0.01	0.05	0.01	0.03	0.02
10	0.02	0.04	0.01	0.02	0.01	0.05	0.09	0.01	0.03	0.03
11	0.01	0.04	0.04	0.02	0.01	0.01	0.10	0.01	0.03	0.03
12	0.01	0.03	0.01	0.03	0.02	0.01	0.04	0.03	0.02	0.01
13	0.01	0.01	0.02	0.03	0.01	0.02	0.05	0.02	0.02	0.01
14	0.01	0.02	0.01	0.01	0.01	E.C.	0.03	0.02	0.02	0.01
15	0.01	0.02	0.01	0.02	0.01	0.01	0.06	0.01	0.02	0.02
16	0.01	0.02	0.01	0.01	0.01	0.01	0.03	0.02	0.01	0.01
17	0.01	0.01	0.01	0.01	0.00	0.01	0.14	0.01	0.03	0.05
18	0.01	0.01	0.01	0.01	0.00	0.01	0.02	0.01	0.01	0.01
19	0.01	0.02	0.03	0.01	0.01	E.C.	0.09	0.01	0.02	0.03
20	0.00	0.01	0.01	0.01	E.C.	E.C.	0.05	0.01	0.01	0.02

E.C. = Epidermal Content

TABLE 30 Distribution of Radioactivity (% Applied Dose) at 24 h Post Dose Following Topical Application of [^{14}C]-Fenpropidin in Spray Dilution 2 (1.375 g/L) to Human Split-Thickness Membranes

	Cell Number and Donor Number									
	Cell 41 1362	Cell 42 1362	Cell 43 1418	Cell 44 1418	Cell 45 1371	Cell 46 1371	*Cell 47* *1347*	Cell 48 1347	Mean	SD
Skin Wash 6 h	41.01	28.73	34.81	37.48	29.73	44.83	*22.76*	38.59	36.45	5.83
Tissue Swab 6 h	32.88	36.29	26.12	32.84	46.56	33.59	*33.49*	32.89	34.45	6.16
Pipette Tip 6 h	0.95	0.02	0.11	0.98	0.02	0.04	*0.43*	0.01	0.30	0.45
Filters 6 h	0.59	0.80	2.20	2.79	1.10	0.95	*0.75*	1.18	1.37	0.81
Skin Wash 24 h	4.55	2.69	3.77	3.10	2.67	2.59	*3.01*	1.50	2.98	0.97
Tissue Swab 24 h	1.90	1.66	2.24	0.54	1.26	0.99	*0.62*	0.95	1.36	0.60
Pipette Tip 24 h	0.01	0.01	1.81	0.24	0.01	0.11	*0.65*	0.00	0.31	0.67
Donor Chamber Wash/Trap	0.82	1.51	1.26	0.46	1.22	1.57	*0.30*	1.09	1.13	0.39
Filters 24 h	0.60	0.65	1.02	1.19	0.80	0.53	*0.11*	0.12	0.70	0.35
Stratum Corneum 1-2	0.21	0.10	0.89	0.43	N/S	0.33	*0.06*	0.09	0.34	0.30
Stratum Corneum 3-5	0.12	0.10	0.45	0.32	N/S	0.20	*0.06*	0.05	0.21	0.15
Stratum Corneum 6-10	0.23	0.12	0.16	0.13	N/S	0.12	*0.05*	0.05	0.13	0.06
Stratum Corneum 11-15	0.09	0.07	0.06	0.06	N/S	0.08	*0.03*	0.04	0.07	0.02
Stratum Corneum 16-20	0.09	0.07	0.07	0.03	N/S	0.06	*0.02*	0.03	0.06	0.03
Unexposed Skin	0.30	2.88	0.89	0.23	0.12	0.06	*0.07*	0.39	0.70	1.00
Exposed Skin	3.62	7.43	2.64	1.66	1.05	0.94	*1.18*	2.31	2.81	2.24
Receptor Fluid	7.95	9.14	17.61	10.55	10.04	8.71	*14.02*	13.68	11.10	3.41
Receptor Chamber Wash	0.49	0.87	1.10	0.49	0.47	0.50	*0.49*	0.79	0.67	0.25
Mass Balance	96.40	93.14	97.22	93.52	95.03	96.21	*78.10*	93.76	95.04	1.61

Cell 47 was excluded due to low mass balance
*=Results calculated from data less than 30 d.p.m. above background
°=Mean includes results calculated from data less than 30 d.p.m above background

TABLE 31 **Cumulative Absorption (% Applied Dose) of [^{14}C]-Fenpropidin into Receptor Fluid Following Topical Application of the [^{14}C]-Fenpropidin in Spray Dilution 2 (1.375 g/L) to Human Split-Thickness Membranes**

	Cell Number and Donor Number									
Time (h)	Cell 41 1362	Cell 42 1362	Cell 43 1418	Cell 44 1418	Cell 45 1371	Cell 46 1371	*Cell 47 1347*	Cell 48 1347	Mean	SD
0	0.00	0.00	0.00	0.00	0.00	0.00	*0.00*	0.00	0.00	0.00
2	*0.00	*0.01	0.68	1.40	0.60	0.65	*0.86*	0.51	°0.55	°0.47
4	0.46	0.54	3.46	5.23	2.53	2.98	*3.73*	2.86	2.58	1.67
6	1.42	1.69	6.79	6.98	4.67	4.58	*6.68*	5.43	4.51	2.22
8	2.60	3.75	13.18	8.95	6.47	6.02	*8.39*	8.11	7.01	3.52
12	4.07	6.51	15.84	10.71	8.36	8.10	*10.98*	10.94	9.22	3.76
24	7.95	9.14	17.61	10.55	10.04	8.71	*14.02*	13.68	11.10	3.41

Cell 47 was excluded due to low mass balance
*=Results calculated from data less than 30 d.p.m. above background
°=Mean includes results calculated from data less than 30 d.p.m above background

TABLE 32 **Distribution of Radioactivity (µg equiv./cm^2) at 24 h Post Dose Following Topical Application of [^{14}C]-Fenpropidin in Spray Dilution 2 (1.375 g/L) to Human Split-Thickness Membranes**

	Cell Number and Donor Number									
	Cell 41 1362	Cell 42 1362	Cell 43 1418	Cell 44 1418	Cell 45 1371	Cell 46 1371	*Cell 47* *1347*	Cell 48 1347	Mean	SD
Skin Wash 6 h	5.89	4.12	5.00	5.38	4.27	6.44	*3.27*	5.54	5.23	0.84
Tissue Swab 6 h	4.72	5.21	3.75	4.71	6.68	4.82	*4.81*	4.72	4.95	0.88
Pipette Tip 6 h	0.14	0.00	0.02	0.14	0.00	0.01	*0.06*	0.00	0.04	0.06
Filters 6 h	0.08	0.11	0.32	0.40	0.16	0.14	*0.11*	0.17	0.20	0.12
Skin Wash 24 h	0.65	0.39	0.54	0.45	0.38	0.37	*0.43*	0.22	0.43	0.14
Tissue Swab 24 h	0.27	0.24	0.32	0.08	0.18	0.14	*0.09*	0.14	0.20	0.09
Pipette Tip 24 h	0.00	0.00	0.26	0.04	0.00	0.02	*0.09*	0.00	0.05	0.10
Donor Chamber Wash/Trap	0.12	0.22	0.18	0.07	0.18	0.23	*0.04*	0.16	0.16	0.06
Filters 24 h	0.09	0.09	0.15	0.17	0.11	0.08	*0.02*	0.02	0.10	0.05
Stratum Corneum 1-2	0.03	0.02	0.13	0.06	N/S	0.05	*0.01*	0.01	0.05	0.04
Stratum Corneum 3-5	0.02	0.01	0.06	0.05	N/S	0.03	*0.01*	0.01	0.03	0.02
Stratum Corneum 6-10	0.03	0.02	0.02	0.02	N/S	0.02	*0.01*	0.01	0.02	0.01
Stratum Corneum 11-15	0.01	0.01	0.01	0.01	N/S	0.01	*0.00*	0.01	0.01	0.00
Stratum Corneum 16-20	0.01	0.01	0.01	0.00	N/S	0.01	*0.00*	0.00	0.01	0.00
Unexposed Skin	0.04	0.41	0.13	0.03	0.02	0.01	*0.01*	0.06	0.10	0.14
Exposed Skin	0.52	1.07	0.38	0.24	0.15	0.14	*0.17*	0.33	0.40	0.32
Receptor Fluid	1.14	1.31	2.53	1.52	1.44	1.25	*2.01*	1.96	1.59	0.49
Receptor Chamber Wash	0.07	0.12	0.16	0.07	0.07	0.07	*0.07*	0.11	0.10	0.04
Mass Balance	13.84	13.37	13.96	13.43	13.64	13.81	*11.21*	13.46	13.64	0.23

Cell 47 was excluded due to low mass balance

TABLE 33 **Cumulative Absorption (µg equiv./cm^2) of [^{14}C]-Fenpropidin into Receptor Fluid Following Topical Application of [^{14}C]-Fenpropidin in Spray Dilution 2 (1.375 g/L) to Human Split-Thickness Membranes**

	Cell Number and Donor Number									
Time (h)	Cell 41 1362	Cell 42 1362	Cell 43 1418	Cell 44 1418	Cell 45 1371	Cell 46 1371	*Cell 47 1347*	Cell 48 1347	Mean	SD
0	0.00	0.00	0.00	0.00	0.00	0.00	*0.00*	0.00	0.00	0.00
2	*0.00	*0.00	0.10	0.20	0.09	0.09	*0.12*	0.07	°0.08	°0.07
4	0.07	0.08	0.50	0.75	0.36	0.43	*0.54*	0.41	0.37	0.24
6	0.20	0.24	0.97	1.00	0.67	0.66	*0.96*	0.78	0.65	0.32
8	0.37	0.54	1.89	1.29	0.93	0.86	*1.20*	1.16	1.01	0.51
12	0.58	0.94	2.27	1.54	1.20	1.16	*1.58*	1.57	1.32	0.54
24	1.14	1.31	2.53	1.52	1.44	1.25	*2.01*	1.96	1.59	0.49

Cell 47 was excluded due to low mass balance
*=Results calculated from data less than 30 d.p.m. above background
°=Mean includes results calculated from data less than 30 d.p.m above background

TABLE 34 **Distribution of Radioactivity (µg equiv./cm^2) in the *Stratum Corneum* at 24 h Post Dose Following Topical Application of [^{14}C]-Fenpropidin in Spray Dilution 2 (1.375 g/L) to Human Split-Thickness Membranes**

	Cell Number and Donor Number									
Tape Strip No.	Cell 41 1362	Cell 42 1362	Cell 43 1418	Cell 44 1418	Cell 45 1371	Cell 46 1371	*Cell 47* *1347*	Cell 48 1347	Mean	SD
1	0.018	0.010	0.092	0.041	N/S	0.034	*0.006*	0.008	0.034	0.031
2	0.012	0.005	0.036	0.021	N/S	0.014	*0.003*	0.005	0.015	0.012
3	0.005	0.003	0.030	0.020	N/S	0.015	*0.005*	0.003	0.012	0.011
4	0.007	0.005	0.023	0.012	N/S	0.008	*0.003*	0.003	0.010	0.007
5	0.005	0.007	0.011	0.013	N/S	0.005	**0.002*	*0.002	°0.007	°0.004
6	0.006	0.005	E.C.	0.005	N/S	0.005	**0.000*	*0.001	°0.004	°0.002
7	0.005	0.002	0.009	0.007	N/S	0.005	*0.002*	0.002	0.005	0.003
8	0.015	0.003	0.003	0.004	N/S	0.004	**0.002*	*0.001	°0.005	°0.005
9	0.004	0.003	0.009	0.002	N/S	0.002	**0.001*	*0.001	°0.004	°0.003
10	0.003	0.004	*0.002	*0.001	N/S	*0.002	**0.001*	*0.001	°0.002	°0.001
11	0.004	0.003	0.003	0.003	N/S	*0.002	**0.001*	*0.001	°0.003	°0.001
12	0.005	*0.001	0.002	0.002	N/S	0.002	**0.001*	*0.001	°0.002	°0.001
13	*0.001	*0.001	*0.001	*0.001	N/S	0.004	**0.001*	*0.001	°0.002	°0.001
14	0.002	*0.002	*0.001	*0.001	N/S	*0.001	**0.001*	*0.001	°0.001	°0.001
15	*0.001	0.003	*0.001	*0.001	N/S	*0.002	**0.000*	*0.001	°0.001	°0.001
16	*0.002	*0.001	0.002	*0.000	N/S	*0.001	**0.001*	*0.001	°0.001	°0.001
17	0.004	0.002	*0.001	*0.001	N/S	*0.001	**0.001*	*0.001	°0.002	°0.001
18	0.004	0.003	*0.001	*0.001	N/S	E.C.	**0.001*	*0.001	°0.002	°0.001
19	0.002	*0.002	*0.001	*0.001	N/S	0.002	**0.000*	*0.001	°0.002	°0.000
20	0.002	*0.001	0.004	*0.001	N/S	0.004	**0.001*	*0.001	°0.002	°0.002

Cell 47 was excluded due to low mass balance
E.C. = Epidermal Content
N/S = No Sample
*=Results calculated from data less than 30 d.p.m. above background
°=Mean includes results calculated from data less than 30 d.p.m above background

TABLE 35 **Distribution of [^{14}C]-Propiconazole (% Applied Dose and µg equiv./cm^2) in Tissue Swabs at 6 h Post Dose Following Topical Application of Formulation Concentrate (125 g/L), Spray Dilution 1 (6.25 g/L) and Spray Dilution 2 (0.625 g/L) to Human Split-Thickness Membranes**

Formulation Concentrate

% Applied Dose

	Cell Number and Donor Number							
	Cell 1 (1357)	*Cell 2 (1357)*	*Cell 3 (1382)*	Cell 4 (1382)	*Cell 5 (1368)*	Cell 6 (1368)	Cell 7 (1472)	Cell 8 (1472)
6 h Tissue Swab 1	*73.76*	*43.49*	*28.35*	81.08	*51.02*	56.73	73.01	51.95
6 h Tissue Swab 2	*1.19*	*1.08*	*6.00*	1.61	*2.96*	2.11	1.33	3.48
6 h Tissue Swab 3	*1.33*	*1.47*	*0.98*	0.62	*1.95*	0.46	1.57	0.54
6 h Tissue Swab 4	*0.17*	*0.46*	*1.15*	0.11	*0.61*	0.56	0.52	0.45
6 h Tissue Swab 5	*0.01*	*0.01*	*0.09*	0.01	*0.03*	0.07	0.03	0.02
Total	*76.46*	*46.51*	*36.58*	83.44	*56.59*	59.93	76.46	56.43

	Cell Number and Donor Number									
	Cell 69 (1370)	Cell 70 (1370)	Cell 71 (1445)	Cell 72 (1445)	Cell 73 (1344)	Cell 74 (1344)	Cell 75 (1449)	Cell 76 (1449)	Mean	SD
6 h Tissue Swab 1	60.48	45.89	43.02	75.41	44.34	65.66	44.10	29.41	55.92	15.61
6 h Tissue Swab 2	2.06	4.41	8.32	1.31	1.16	4.54	3.43	0.66	2.87	2.15
6 h Tissue Swab 3	2.38	0.52	1.58	1.22	0.22	0.33	2.92	0.35	1.06	0.89
6 h Tissue Swab 4	0.80	1.16	0.50	0.44	0.18	0.61	0.64	0.06	0.50	0.30
6 h Tissue Swab 5	0.15	0.04	0.24	0.12	0.01	0.20	0.10	0.01	0.08	0.08
Total	65.88	52.01	53.66	78.50	45.92	71.35	51.19	30.49	60.44	15.34

Cells 1, 2, 3 and 5 were excluded due to low mass balance

µg equiv./cm^2

	Cell Number and Donor Number							
	Cell 1 (1357)	*Cell 2 (1357)*	*Cell 3 (1382)*	Cell 4 (1382)	*Cell 5 (1368)*	Cell 6 (1368)	Cell 7 (1472)	Cell 8 (1472)
6 h Tissue Swab 1	*939.71*	*554.08*	*361.22*	1033.04	*650.07*	722.80	930.17	661.91
6 h Tissue Swab 2	*15.16*	*13.73*	*76.48*	20.53	*37.74*	26.85	17.01	44.33
6 h Tissue Swab 3	*17.00*	*18.71*	*12.55*	7.91	*24.88*	5.90	20.00	6.83
6 h Tissue Swab 4	*2.17*	*5.84*	*14.63*	1.46	*7.83*	7.12	6.64	5.70
6 h Tissue Swab 5	*0.12*	*0.19*	*1.16*	0.11	*0.42*	0.85	0.38	0.23
Total	*974.17*	*592.56*	*466.03*	1063.05	*720.94*	763.51	974.20	719.00

	Cell Number and Donor Number									
	Cell 69 (1370)	Cell 70 (1370)	Cell 71 (1445)	Cell 72 (1445)	Cell 73 (1344)	Cell 74 (1344)	Cell 75 (1449)	Cell 76 (1449)	Mean	SD
6 h Tissue Swab 1	771.22	585.11	548.56	961.53	565.44	837.28	562.28	375.07	712.87	198.85
6 h Tissue Swab 2	26.29	56.22	106.08	16.74	14.83	57.89	43.74	8.41	36.58	27.44
6 h Tissue Swab 3	30.41	6.64	20.19	15.57	2.79	4.16	37.25	4.43	13.51	11.30
6 h Tissue Swab 4	10.23	14.75	6.38	5.60	2.35	7.84	8.19	0.73	6.42	3.86
6 h Tissue Swab 5	1.95	0.48	3.04	1.56	0.14	2.56	1.23	0.12	1.05	1.02
Total	840.10	663.19	684.25	1001.00	585.55	909.74	652.69	388.77	770.42	195.38

Cells 1, 2, 3 and 5 were excluded due to low mass balance

Spray Dilution 1

% Applied Dose

	Cell Number and Donor Number							
	Cell 9 (1357)	Cell 10 (1357)	Cell 11 (1382)	*Cell 12 (1382)*	Cell 13 (1368)	Cell 14 (1368)	*Cell 15 (1472)*	Cell 16 (1472)
6 h Tissue Swab 1	39.53	44.30	31.86	*32.32*	50.75	31.41	*27.78*	49.61
6 h Tissue Swab 2	5.42	2.67	7.92	*9.76*	2.95	5.95	*4.37*	4.23
6 h Tissue Swab 3	1.20	4.79	2.86	*5.48*	2.89	2.64	*1.47*	5.07
6 h Tissue Swab 4	1.93	1.16	1.34	*1.34*	1.44	1.55	*1.72*	0.98
6 h Tissue Swab 5	0.15	0.07	0.12	*0.06*	0.06	0.25	*0.06*	0.15
Total	48.23	53.00	44.10	*48.96*	58.08	41.79	*35.40*	60.04

	Cell Number and Donor Number									
	Cell 77 (1370)	Cell 78 (1370)	Cell 79 (1445)	Cell 80 (1445)	Cell 81 (1344)	Cell 82 (1344)	Cell 83 (1449)	Cell 84 (1449)	Mean	SD
6 h Tissue Swab 1	38.84	39.58	31.73	38.80	29.95	27.22	43.81	39.80	41.24	8.45
6 h Tissue Swab 2	7.92	7.43	5.38	5.67	3.97	4.87	7.13	4.19	4.86	1.98
6 h Tissue Swab 3	3.42	1.83	2.96	0.98	3.20	1.03	1.90	2.81	3.24	1.45
6 h Tissue Swab 4	1.67	2.89	0.74	1.03	1.78	0.84	1.28	1.46	1.40	0.33
6 h Tissue Swab 5	0.22	0.17	0.07	0.06	0.14	0.04	0.33	0.06	0.13	0.07
Total	52.07	51.90	40.87	46.54	39.03	33.99	54.44	48.31	50.87	7.43

Cells 12 and 15 were excluded due to low mass balance

µg equiv./cm^2

	Cell Number and Donor Number							
	Cell 9 (1357)	Cell 10 (1357)	Cell 11 (1382)	*Cell 12 (1382)*	Cell 13 (1368)	Cell 14 (1368)	*Cell 15 (1472)*	Cell 16 (1472)
6 h Tissue Swab 1	25.70	28.80	20.71	*21.01*	32.99	20.42	*18.06*	32.25
6 h Tissue Swab 2	3.52	1.74	5.15	*6.35*	1.92	3.87	*2.84*	2.75
6 h Tissue Swab 3	0.78	3.12	1.86	*3.56*	1.88	1.72	*0.96*	3.30
6 h Tissue Swab 4	1.26	0.76	0.87	*0.87*	0.93	1.01	*1.12*	0.64
6 h Tissue Swab 5	0.10	0.05	0.08	*0.04*	0.04	0.16	*0.04*	0.10
Total	31.35	34.45	28.67	*31.83*	37.76	27.17	*23.01*	39.03

	Cell Number and Donor Number									
	Cell 77 (1370)	Cell 78 (1370)	Cell 79 (1445)	Cell 80 (1445)	Cell 81 (1344)	Cell 82 (1344)	Cell 83 (1449)	Cell 84 (1449)	Mean	SD
6 h Tissue Swab 1	23.06	23.50	18.84	23.04	17.78	16.16	26.01	23.63	23.78	5.04
6 h Tissue Swab 2	4.70	4.41	3.19	3.37	2.36	2.89	4.23	2.49	3.33	1.05
6 h Tissue Swab 3	2.03	1.09	1.76	0.58	1.90	0.61	1.13	1.67	1.67	0.82
6 h Tissue Swab 4	0.99	1.71	0.44	0.61	1.06	0.50	0.76	0.87	0.89	0.33
6 h Tissue Swab 5	0.13	0.10	0.04	0.04	0.08	0.02	0.19	0.03	0.08	0.05
Total	30.92	30.82	24.27	27.64	23.18	20.18	32.33	28.69	29.75	5.28

Cells 12 and 15 were excluded due to low mass balance

Spray Dilution 2

% Applied dose

	Cell Number and Donor Number									
	Cell 17 (1357)	Cell 18 (1357)	Cell 19 (1382)	*Cell 20 (1382)*	Cell 21 (1368)	Cell 22 (1368)	Cell 23 (1472)	Cell 24 (1472)	Mean	SD
6 h Tissue Swab 1	19.10	21.47	28.20	*31.49*	26.23	42.24	15.44	25.72	25.49	8.63
6 h Tissue Swab 2	4.93	5.82	2.18	*2.42*	3.31	1.94	6.96	2.81	3.99	1.93
6 h Tissue Swab 3	2.33	1.88	1.64	*1.90*	1.77	2.17	4.91	2.36	2.44	1.13
6 h Tissue Swab 4	2.51	1.67	0.87	*0.85*	1.43	0.59	2.30	1.62	1.57	0.69
6 h Tissue Swab 5	0.10	0.07	0.15	*0.04*	0.10	0.07	0.35	0.09	0.13	0.10
Total	28.97	30.92	33.04	*36.69*	32.84	47.01	29.97	32.60	33.62	6.11

Cell 20 was excluded due to low mass balance

µg equiv./cm^2

	Cell Number and Donor Number									
	Cell 17 (1357)	Cell 18 (1357)	Cell 19 (1382)	*Cell 20 (1382)*	Cell 21 (1368)	Cell 22 (1368)	Cell 23 (1472)	Cell 24 (1472)	Mean	SD
6 h Tissue Swab 1	1.27	1.43	1.87	*2.09*	1.74	2.81	1.03	1.71	1.69	0.57
6 h Tissue Swab 2	0.33	0.39	0.14	*0.16*	0.22	0.13	0.46	0.19	0.27	0.13
6 h Tissue Swab 3	0.15	0.13	0.11	*0.13*	0.12	0.14	0.33	0.16	0.16	0.07
6 h Tissue Swab 4	0.17	0.11	0.06	*0.06*	0.09	0.04	0.15	0.11	0.10	0.05
6 h Tissue Swab 5	0.01	0.00	0.01	*0.00*	0.01	0.00	0.02	0.01	0.01	0.01
Total	1.92	2.05	2.20	*2.44*	2.18	3.12	1.99	2.17	2.23	0.41

Cell 20 was excluded due to low mass balance

TABLE 36 **Distribution of [^{14}C]-Fenpropidin (% Applied Dose and µg equiv./cm^2) in Tissue Swabs at 6 h Post Dose Following Topical Application of Formulation Concentrate (275 g/L), Spray Dilution 1 (13.75 g/L) and Spray Dilution 2 (1.375 g/L) to Human Split-Thickness Membranes**

Formulation Concentrate

% Applied dose

	Cell Number and Donor Number							
	Cell 25 (1362)	Cell 26 (1362)	*Cell 27 (1418)*	Cell 28 (1418)	Cell 29 (1371)	Cell 30 (1371)	Cell 31 (1347)	*Cell 32 (1347)*
6 h Tissue Swab 1	60.87	42.68	*7.83*	57.62	53.01	19.73	52.46	*27.40*
6 h Tissue Swab 2	4.14	5.38	*2.87*	1.52	1.56	3.28	0.90	*3.27*
6 h Tissue Swab 3	1.19	1.48	*0.22*	0.47	0.78	0.37	3.21	*2.29*
6 h Tissue Swab 4	0.65	0.82	*0.66*	0.33	0.36	1.41	0.23	*0.43*
6 h Tissue Swab 5	0.38	0.12	*0.02*	0.15	0.02	0.04	0.03	*0.10*
Total	67.22	50.48	*11.59*	60.10	55.72	24.83	56.84	*33.48*

	Cell Number and Donor Number									
	Cell 61 (1370)	Cell 62 (1370)	Cell 63 (1445)	Cell 64 (1445)	Cell 65 (1344)	Cell 66 (1344)	Cell 67 (1449)	Cell 68 (1449)	Mean	SD
6 h Tissue Swab 1	48.52	56.22	76.74	56.43	58.39	70.14	45.32	42.48	52.90	13.57
6 h Tissue Swab 2	2.88	1.52	2.89	2.91	4.38	2.66	1.12	5.26	2.88	1.48
6 h Tissue Swab 3	0.66	1.28	0.43	0.40	1.07	0.52	0.63	2.51	1.07	0.85
6 h Tissue Swab 4	0.30	0.68	0.48	0.46	0.41	0.71	0.11	0.45	0.53	0.32
6 h Tissue Swab 5	0.56	0.03	0.20	0.06	0.02	0.24	0.01	0.16	0.14	0.16
Total	52.93	59.73	80.74	60.27	64.27	74.27	47.19	50.86	57.53	13.22

Cells 27 and 32 were excluded due to low mass balance

µg equiv./cm^2

	Cell Number and Donor Number							
	Cell 25 (1362)	Cell 26 (1362)	*Cell 27 (1418)*	Cell 28 (1418)	Cell 29 (1371)	Cell 30 (1371)	Cell 31 (1347)	*Cell 32 (1347)*
6 h Tissue Swab 1	1673.08	1173.29	*215.12*	1583.99	1457.07	542.33	1442.15	*753.19*
6 h Tissue Swab 2	113.72	147.75	*78.75*	41.77	42.85	90.11	24.71	*89.82*
6 h Tissue Swab 3	32.68	40.65	*5.93*	13.02	21.56	10.14	88.34	*62.98*
6 h Tissue Swab 4	17.92	22.60	*18.04*	8.96	9.82	38.79	6.31	*11.78*
6 h Tissue Swab 5	10.38	3.34	*0.61*	4.18	0.43	1.10	0.84	*2.65*
Total	1847.79	1387.63	*318.45*	1651.92	1531.73	682.47	1562.35	*920.42*

	Cell Number and Donor Number									
	Cell 61 (1370)	Cell 62 (1370)	Cell 63 (1445)	Cell 64 (1445)	Cell 65 (1344)	Cell 66 (1344)	Cell 67 (1449)	Cell 68 (1449)	Mean	SD
6 h Tissue Swab 1	1333.45	1545.00	2109.19	1550.97	1604.74	1927.75	1245.51	1167.56	1454.01	373.05
6 h Tissue Swab 2	79.22	41.89	79.34	79.91	120.28	73.10	30.87	144.61	79.29	40.60
6 h Tissue Swab 3	18.24	35.31	11.91	11.09	29.39	14.42	17.42	68.92	29.51	23.27
6 h Tissue Swab 4	8.31	18.81	13.06	12.74	11.32	19.39	3.12	12.29	14.53	8.85
6 h Tissue Swab 5	15.49	0.69	5.56	1.68	0.50	6.63	0.14	4.46	3.96	4.45
Total	1454.72	1641.69	2219.05	1656.39	1766.24	2041.29	1297.07	1397.84	1581.30	363.37

Cells 27 and 32 were excluded due to low mass balance

Spray Dilution 1

% Applied dose

	Cell Number and Donor Number									
	Cell 33 (1362)	Cell 34 (1362)	Cell 35 (1418)	Cell 36 (1418)	Cell 37 (1371)	Cell 38 (1371)	Cell 39 (1347)	Cell 40 (1347)	Mean	SD
6 h Tissue Swab 1	43.79	28.50	40.15	28.19	34.11	28.90	36.54	47.61	35.97	7.41
6 h Tissue Swab 2	9.38	7.17	3.14	4.77	1.89	7.68	7.44	0.84	5.29	3.09
6 h Tissue Swab 3	2.22	8.33	1.09	0.96	0.97	7.61	0.75	4.56	3.31	3.14
6 h Tissue Swab 4	2.60	2.28	0.81	1.95	1.20	0.57	0.37	0.32	1.26	0.90
6 h Tissue Swab 5	0.27	0.50	0.23	0.13	0.11	0.22	0.03	0.70	0.27	0.22
Total	58.25	46.78	45.42	35.99	38.29	44.98	45.13	54.04	46.11	7.34

µg equiv./cm^2

	Cell Number and Donor Number									
	Cell 33 (1362)	Cell 34 (1362)	Cell 35 (1418)	Cell 36 (1418)	Cell 37 (1371)	Cell 38 (1371)	Cell 39 (1347)	Cell 40 (1347)	Mean	SD
6 h Tissue Swab 1	64.46	41.95	59.10	41.49	50.21	42.54	53.79	70.09	52.96	10.91
6 h Tissue Swab 2	13.81	10.55	4.62	7.02	2.79	11.31	10.95	1.24	7.79	4.55
6 h Tissue Swab 3	3.26	12.26	1.61	1.42	1.43	11.20	1.11	6.71	4.87	4.62
6 h Tissue Swab 4	3.82	3.36	1.19	2.87	1.77	0.83	0.54	0.47	1.86	1.33
6 h Tissue Swab 5	0.40	0.74	0.34	0.19	0.16	0.33	0.04	1.03	0.40	0.33
Total	85.76	68.87	66.86	52.99	56.36	66.21	66.44	79.55	67.88	10.80

Spray Dilution 2

% Applied dose

	Cell Number and Donor Number									
	Cell 41 (1362)	Cell 42 (1362)	Cell 43 (1418)	Cell 44 (1418)	Cell 45 (1371)	Cell 46 (1371)	*Cell 47 (1347)*	Cell 48 (1347)	Mean	SD
6 h Tissue Swab 1	22.22	23.08	21.58	23.28	40.84	25.88	*28.05*	27.41	26.33	6.73
6 h Tissue Swab 2	6.18	9.90	2.70	4.00	3.96	3.75	*2.13*	3.80	4.90	2.44
6 h Tissue Swab 3	2.18	2.48	0.70	4.82	0.90	2.28	*0.36*	1.28	2.09	1.39
6 h Tissue Swab 4	1.96	0.77	0.84	0.66	0.71	0.74	*1.49*	0.26	0.85	0.53
6 h Tissue Swab 5	0.33	0.06	0.30	0.08	0.15	0.93	*1.45*	0.13	0.29	0.30
Total	32.88	36.29	26.12	32.84	46.56	33.59	*33.49*	32.89	34.45	6.16

Cell 47 was excluded due to low mass balance

µg equiv./cm^2

	Cell Number and Donor Number									
	Cell 41 (1362)	Cell 42 (1362)	Cell 43 (1418)	Cell 44 (1418)	Cell 45 (1371)	Cell 46 (1371)	*Cell 47 (1347)*	Cell 48 (1347)	Mean	SD
6 h Tissue Swab 1	3.19	3.31	3.10	3.34	5.86	3.72	*4.03*	3.93	3.78	0.97
6 h Tissue Swab 2	0.89	1.42	0.39	0.57	0.57	0.54	*0.31*	0.55	0.70	0.35
6 h Tissue Swab 3	0.31	0.36	0.10	0.69	0.13	0.33	*0.05*	0.18	0.30	0.20
6 h Tissue Swab 4	0.28	0.11	0.12	0.09	0.10	0.11	*0.21*	0.04	0.12	0.08
6 h Tissue Swab 5	0.05	0.01	0.04	0.01	0.02	0.13	*0.21*	0.02	0.04	0.04
Total	4.72	5.21	3.75	4.71	6.68	4.82	*4.81*	4.72	4.95	0.88

Cell 47 was excluded due to low mass balance

FIGURES SECTION

FIGURE 1 **Individual Absorption Profiles for [^{14}C]-Propiconazole (% Applied Dose) in Receptor Fluid Following Topical Application of [^{14}C]-Propiconazole in Formulation Concentrate (125 g/L) to Human Split-Thickness Membranes**

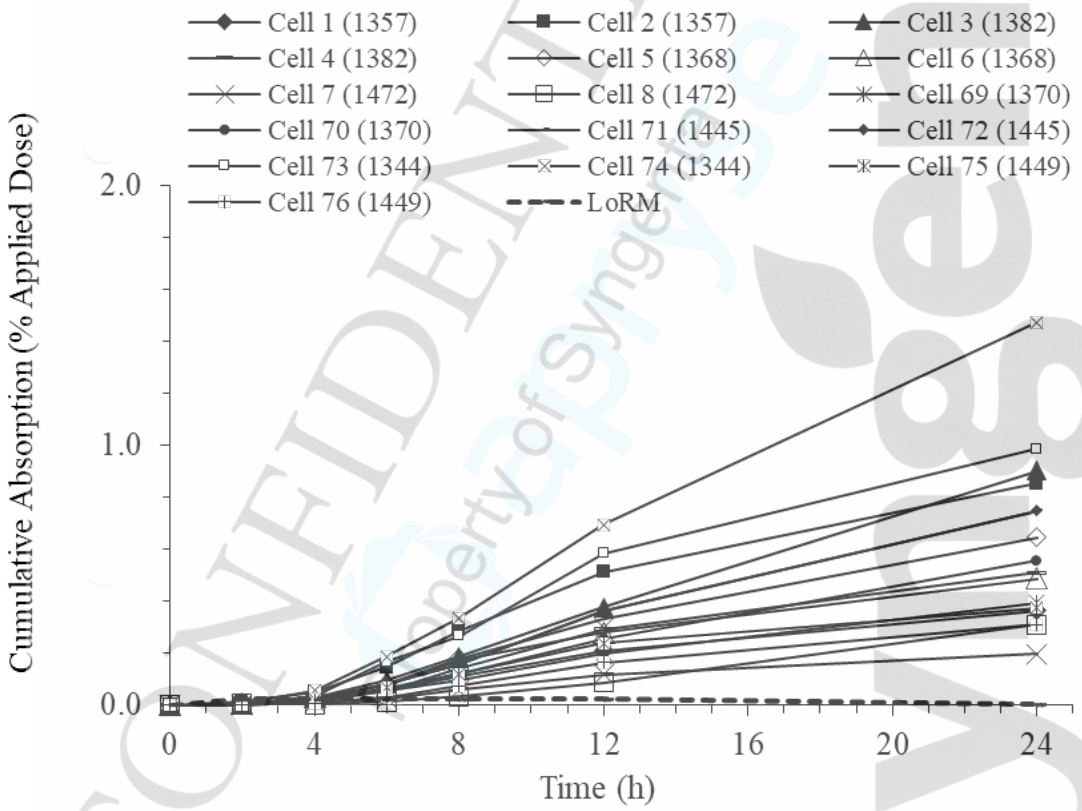


FIGURE 2 **Individual Absorption Profiles for [^{14}C]-Propiconazole (% Applied Dose) in Receptor Fluid Following Topical Application of [^{14}C]-Propiconazole in Formulation Concentrate (125 g/L) to Human Split-Thickness Membranes (Excluding Cells 1, 2, 3 and 5)**

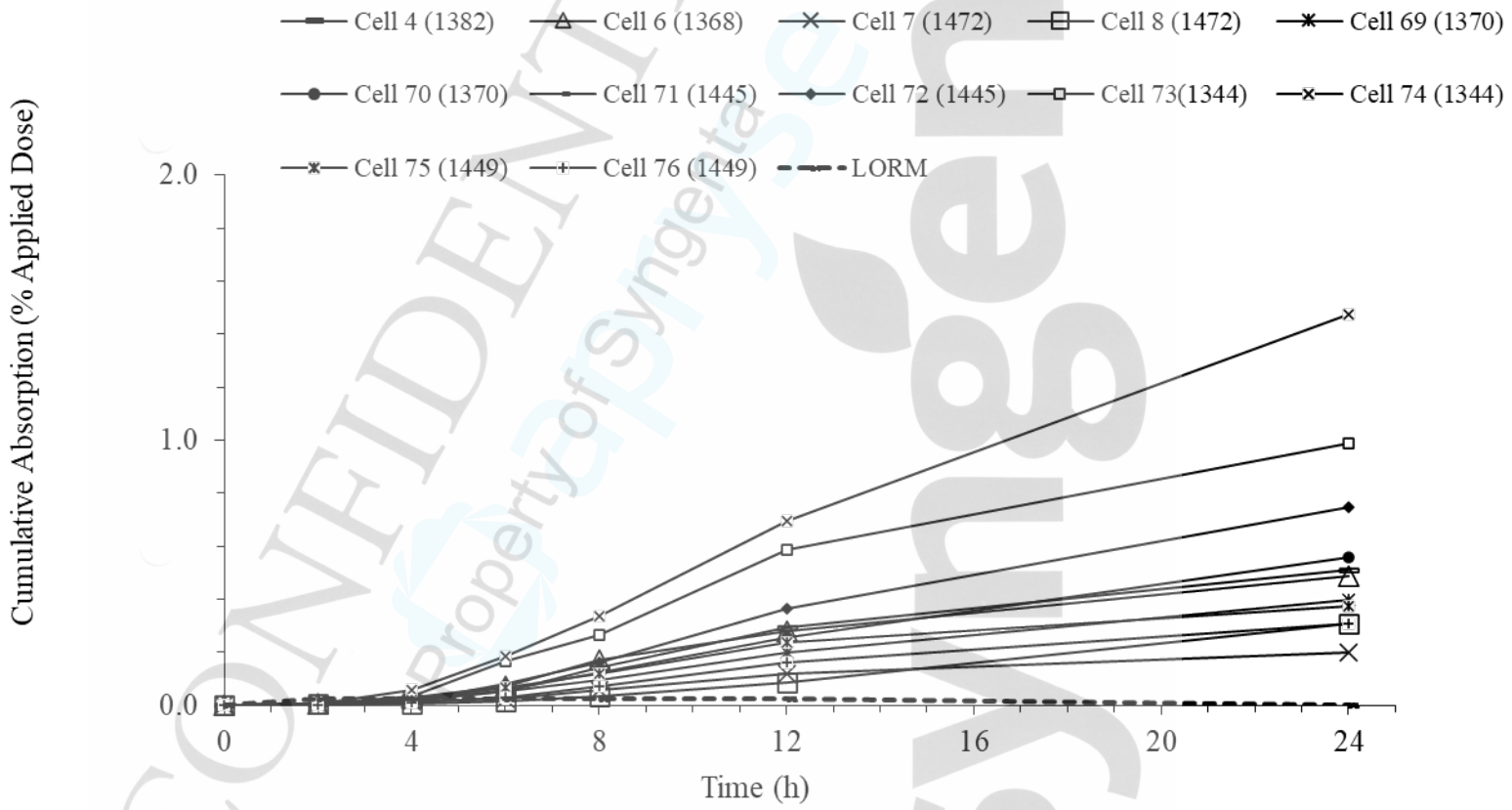


FIGURE 3 **Absorption Profile for [^{14}C]-Propiconazole (% Applied Dose) in Receptor Fluid Following Topical Application of [^{14}C]-Propiconazole in Formulation Concentrate (125 g/L) to Human Split-Thickness Membranes (Mean + SD, n = 12)**

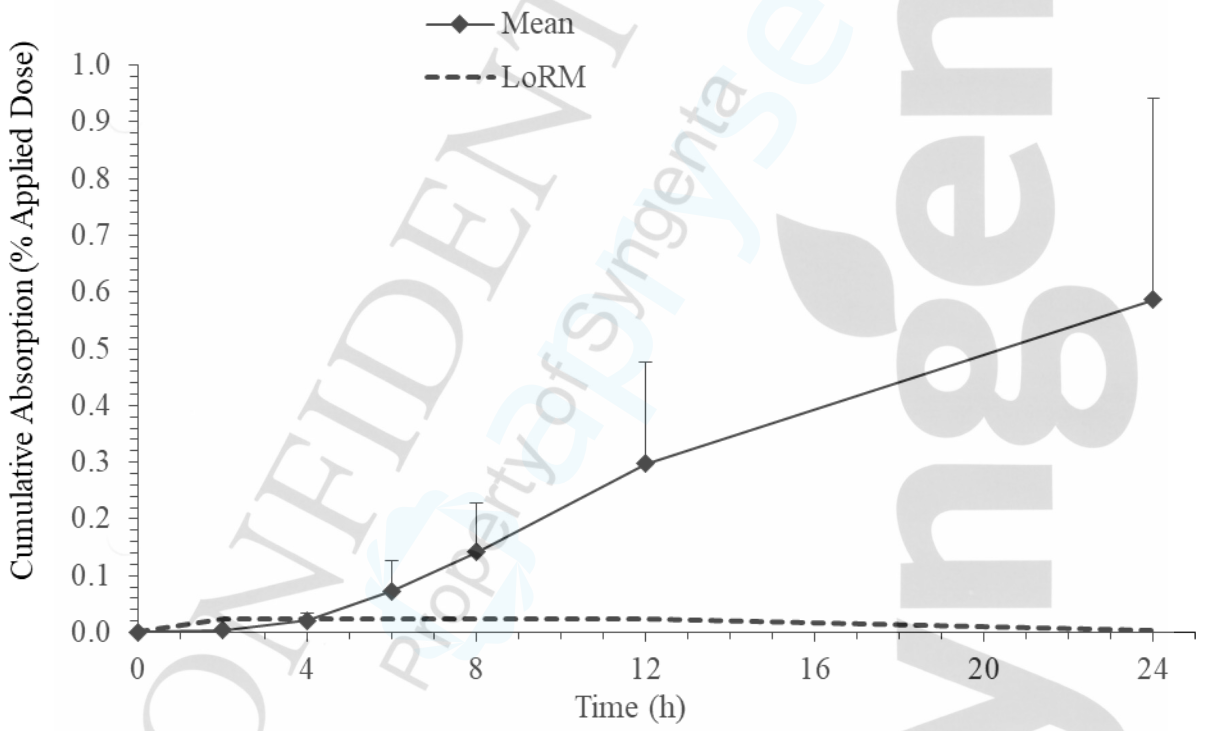


FIGURE 4 **Absorption Profile for [^{14}C]-Propiconazole (µg equiv./cm^2) in Receptor Fluid Following Topical Application of [^{14}C]-Propiconazole in Formulation Concentrate (125 g/L) to Human Split-Thickness Membranes (Mean + SD, n = 12)**

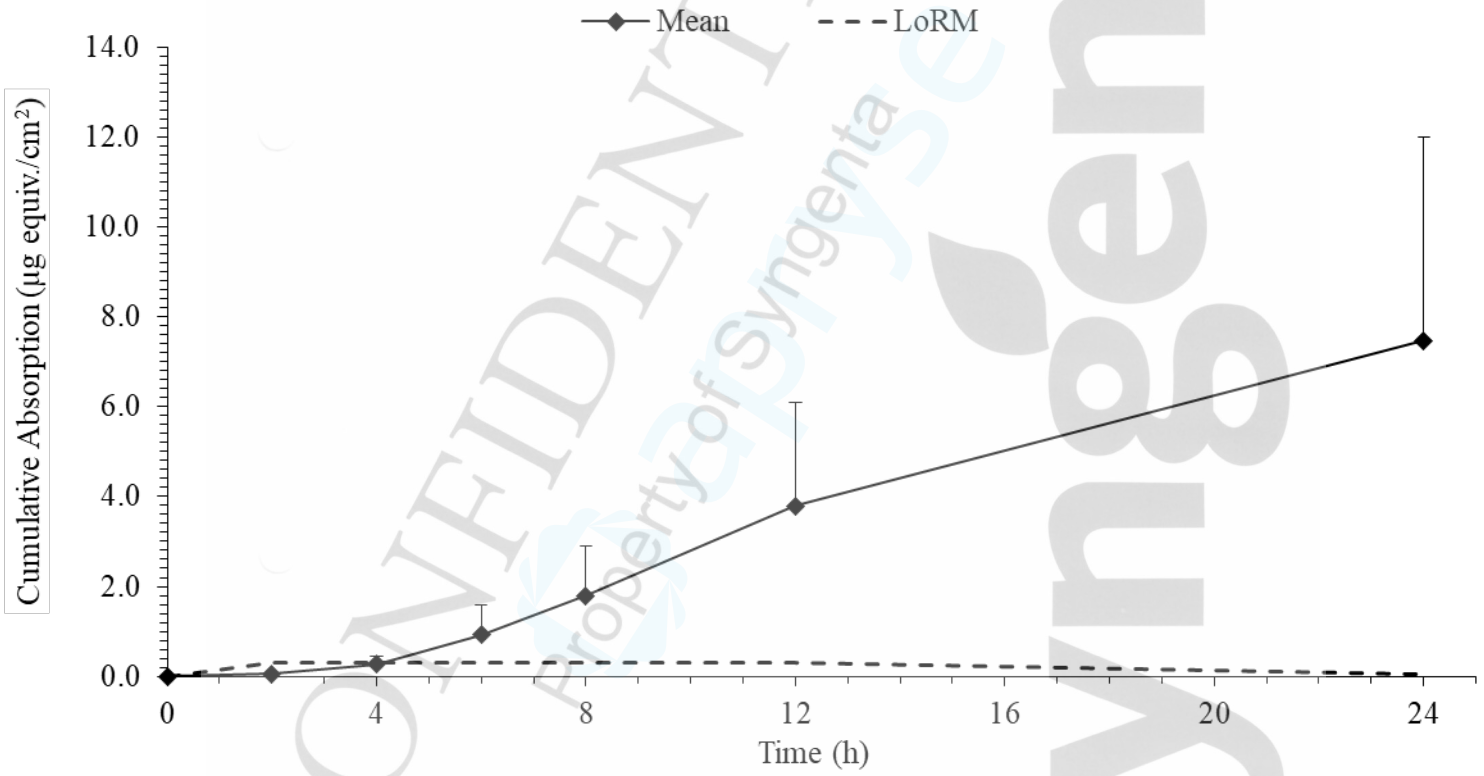


FIGURE 5 **Distribution of [^{14}C]-Propiconazole (µg equiv./cm^2) in the *Stratum Corneum* at 24 h Post Dose Following Topical Application of [^{14}C]-Propiconazole in Formulation Concentrate (125 g/L) to Human Split-Thickness Membranes (Mean + SD, n = 12)**

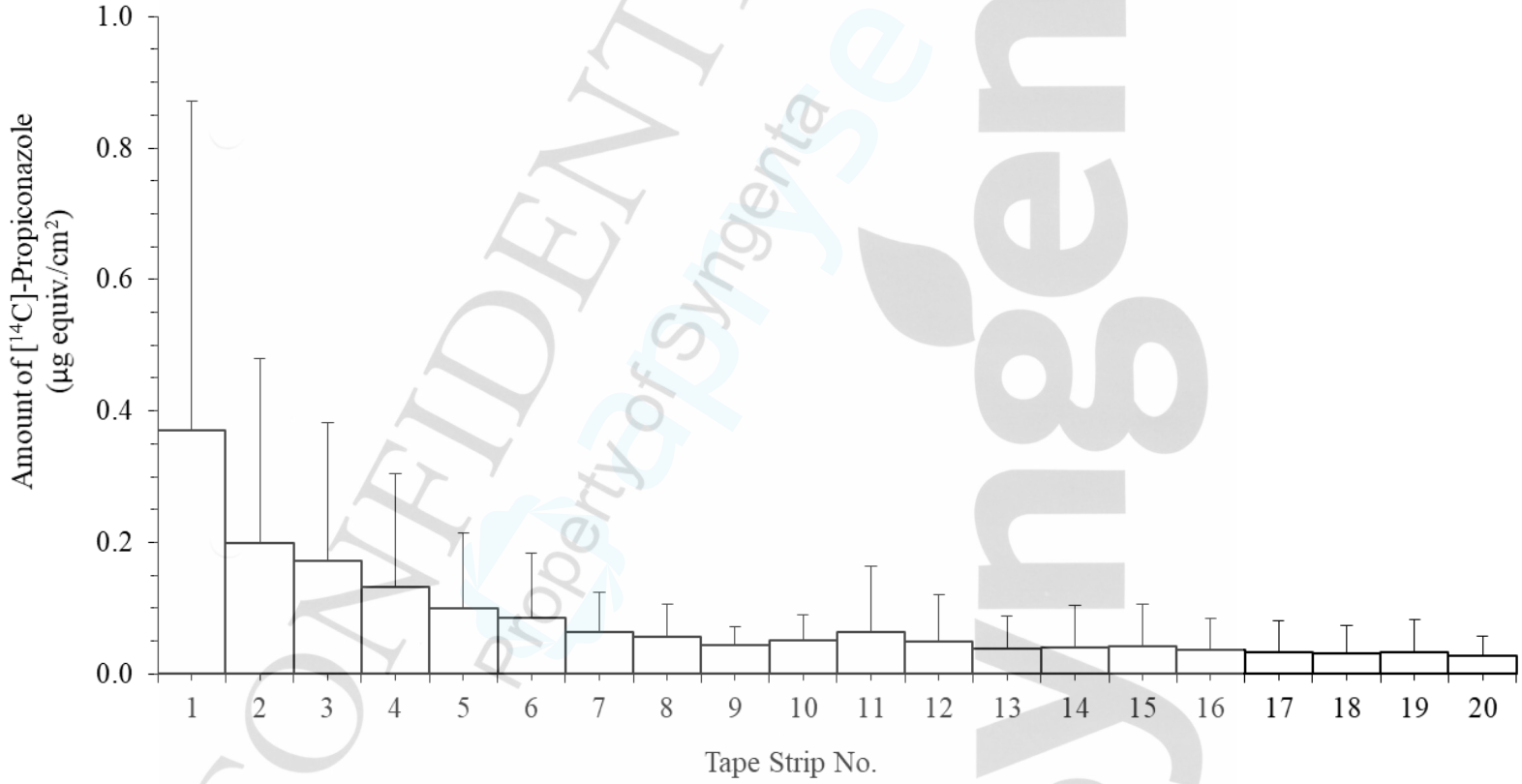


FIGURE 6 **Individual Absorption Profiles for [^{14}C]-Propiconazole (% Applied Dose) in Receptor Fluid Following Topical Application of [^{14}C]-Propiconazole in Spray Dilution 1 (6.25 g/L) to Human Split-Thickness Membranes**

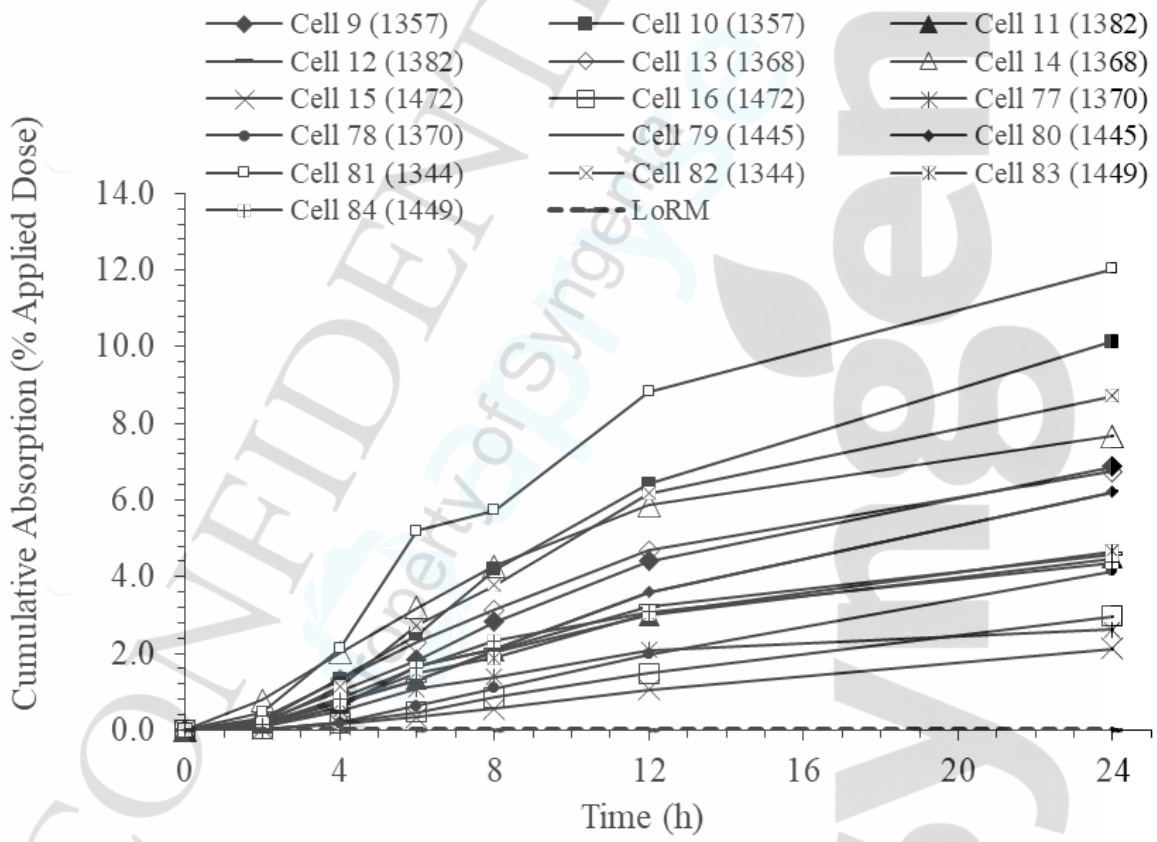


FIGURE 7 **Individual Absorption Profiles for [^{14}C]-Propiconazole (% Applied Dose) in Receptor Fluid Following Topical Application of [^{14}C]-Propiconazole in Spray Dilution 1 (6.25 g/L) to Human Split-Thickness Membranes (Excluding Cells 12 and 15)**

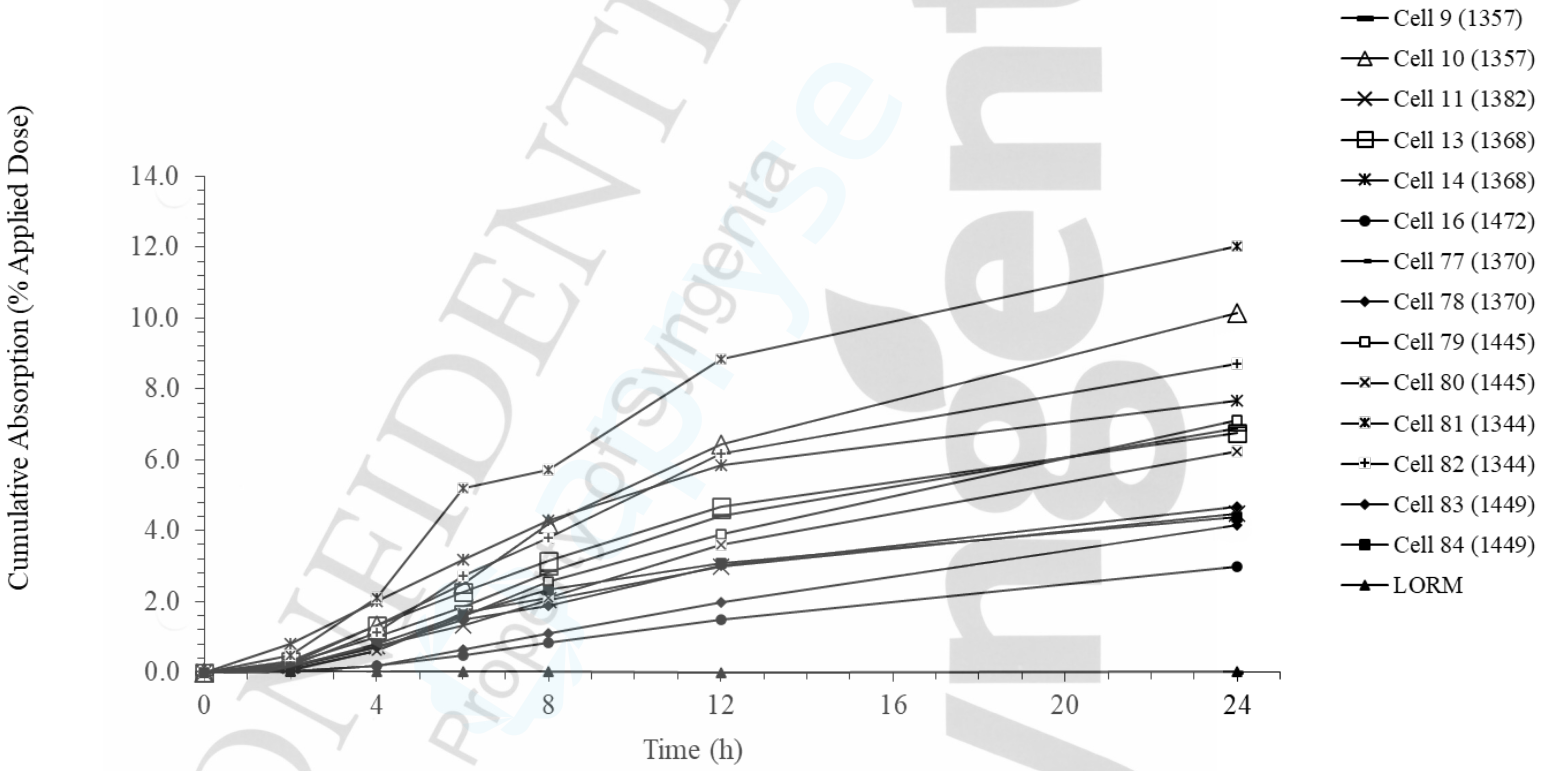


FIGURE 8 **Absorption Profile for [^{14}C]-Propiconazole (% Applied Dose) in Receptor Fluid Following Topical Application of [^{14}C]-Propiconazole in Spray Dilution 1 (6.25 g/L) to Human Split-Thickness Membranes (Mean + SD, n = 14)**

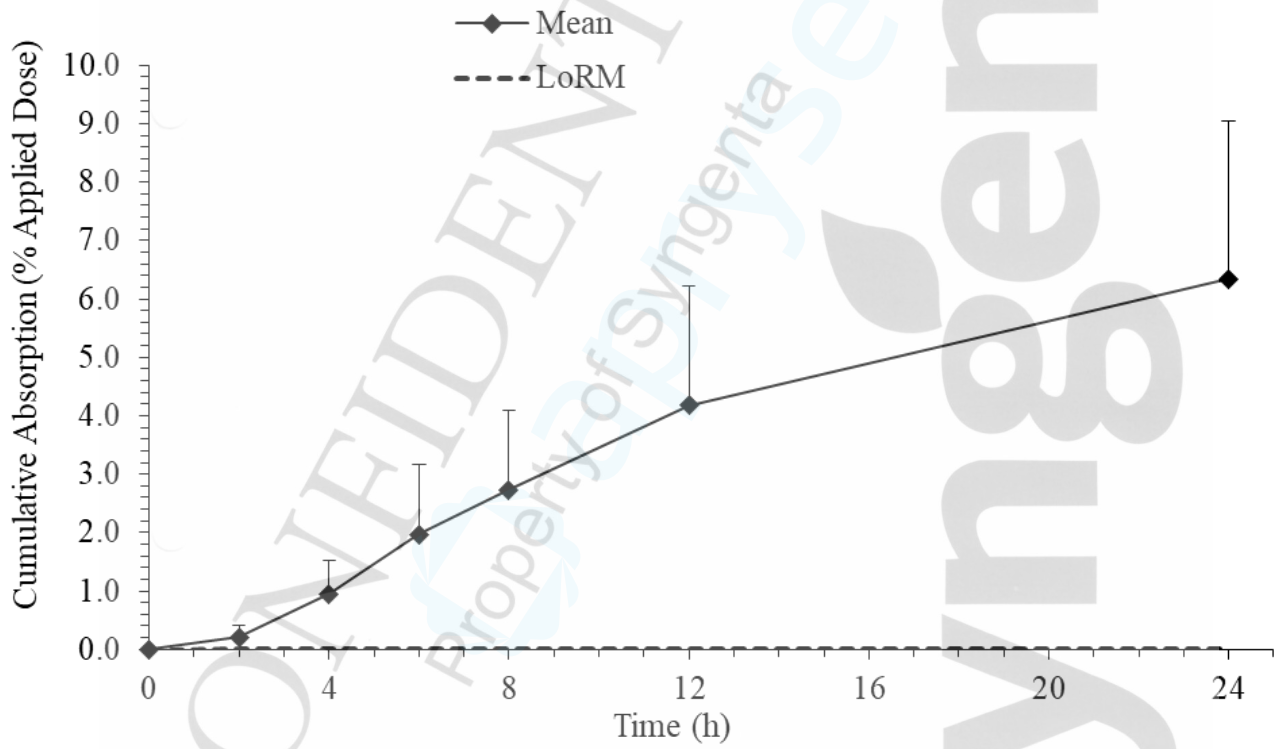


FIGURE 9 **Absorption Profile for [^{14}C]-Propiconazole (µg equiv./cm^2) in Receptor Fluid Following Topical Application of [^{14}C]-Propiconazole in Spray Dilution 1 (6.25 g/L) to Human Split-Thickness Membranes (Mean + SD, n = 14)**

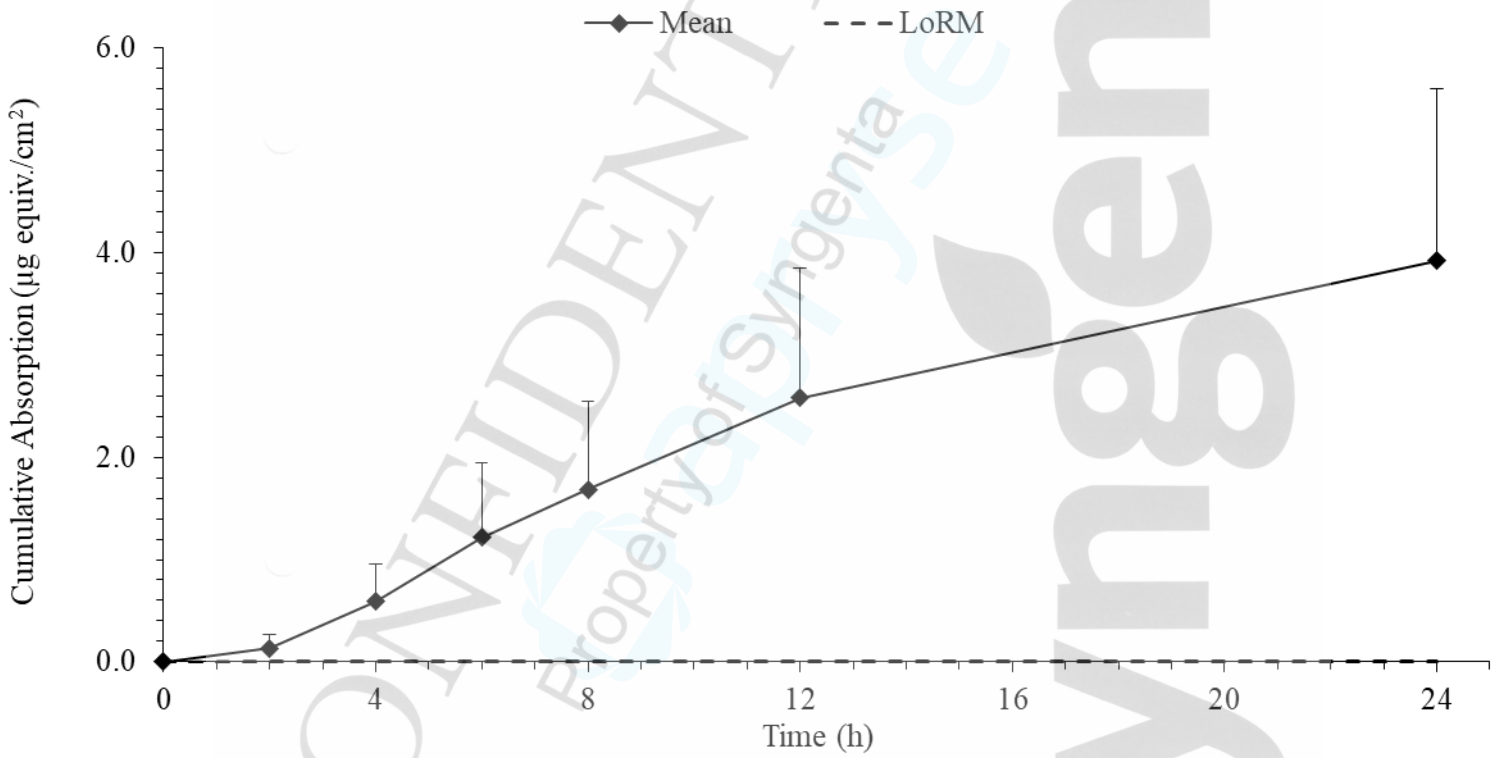


FIGURE 10 **Distribution of [^{14}C]-Propiconazole (µg equiv./cm^2) in the *Stratum Corneum* at 24 h Post Dose Following Topical Application of [^{14}C]-Propiconazole in Spray Dilution 1 (6.25 g/L) to Human Split-Thickness Membranes (Mean + SD, n = 14)**

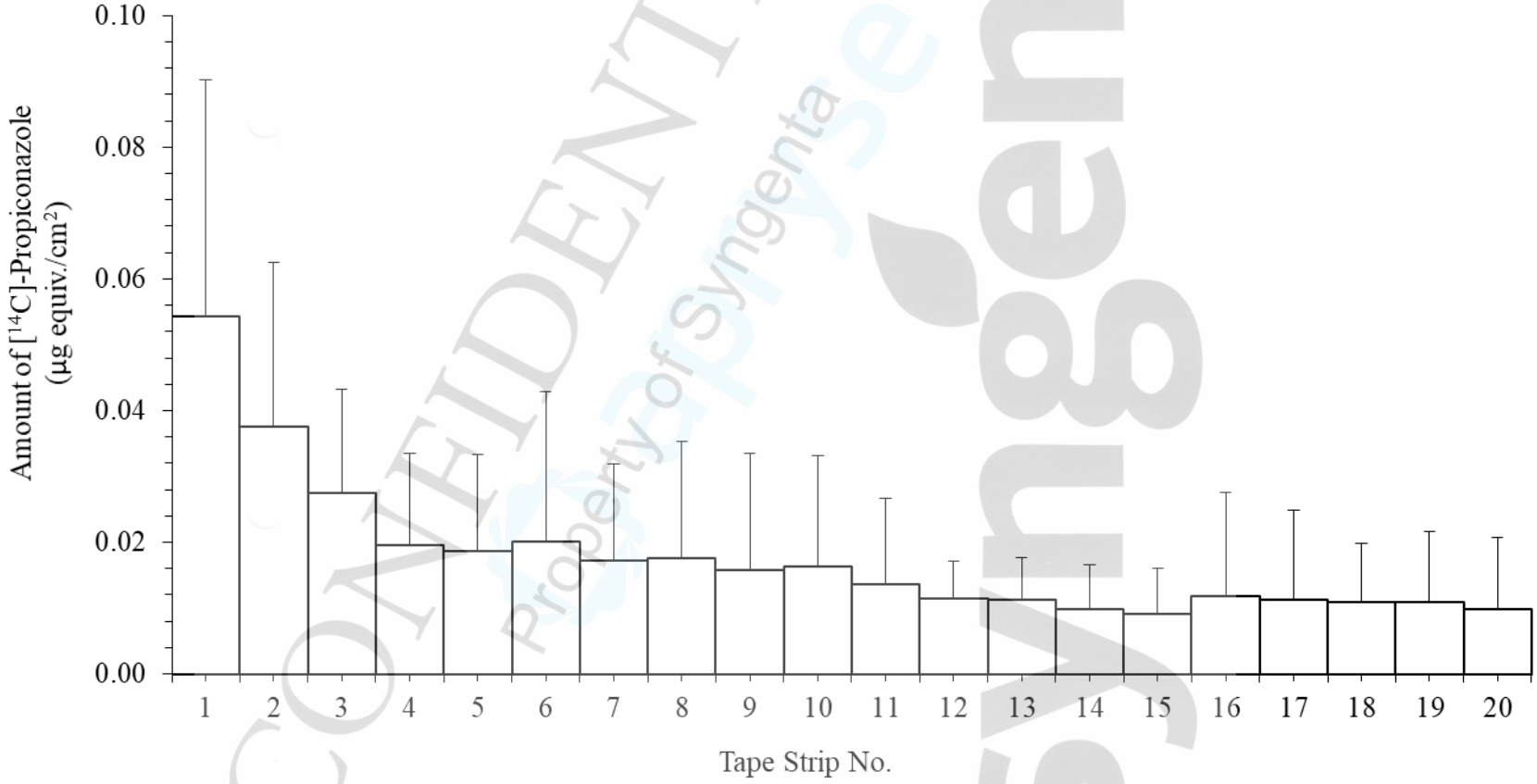


FIGURE 11 **Individual Absorption Profiles for [^{14}C]-Propiconazole (% Applied Dose) in Receptor Fluid Following Topical Application of [^{14}C]-Propiconazole in Spray Dilution 2 (0.625 g/L) to Human Split-Thickness Membranes**

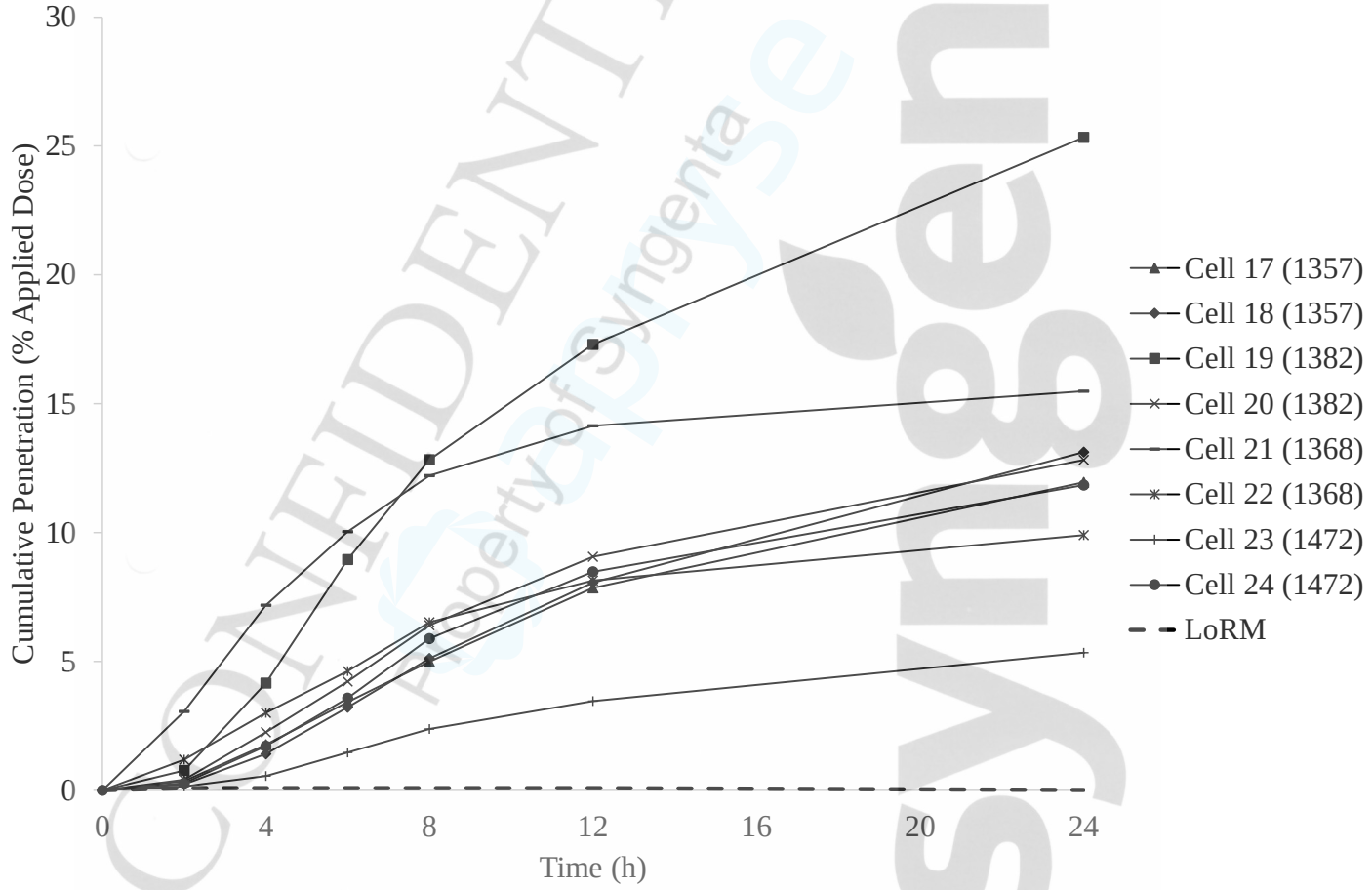


FIGURE 12 **Individual Absorption Profiles for [^{14}C]-Propiconazole (% Applied Dose) in Receptor Fluid Following Topical Application of [^{14}C]-Propiconazole in Spray Dilution 2 (0.625 g/L) to Human Split-Thickness Membranes (Excluding Cell 20)**

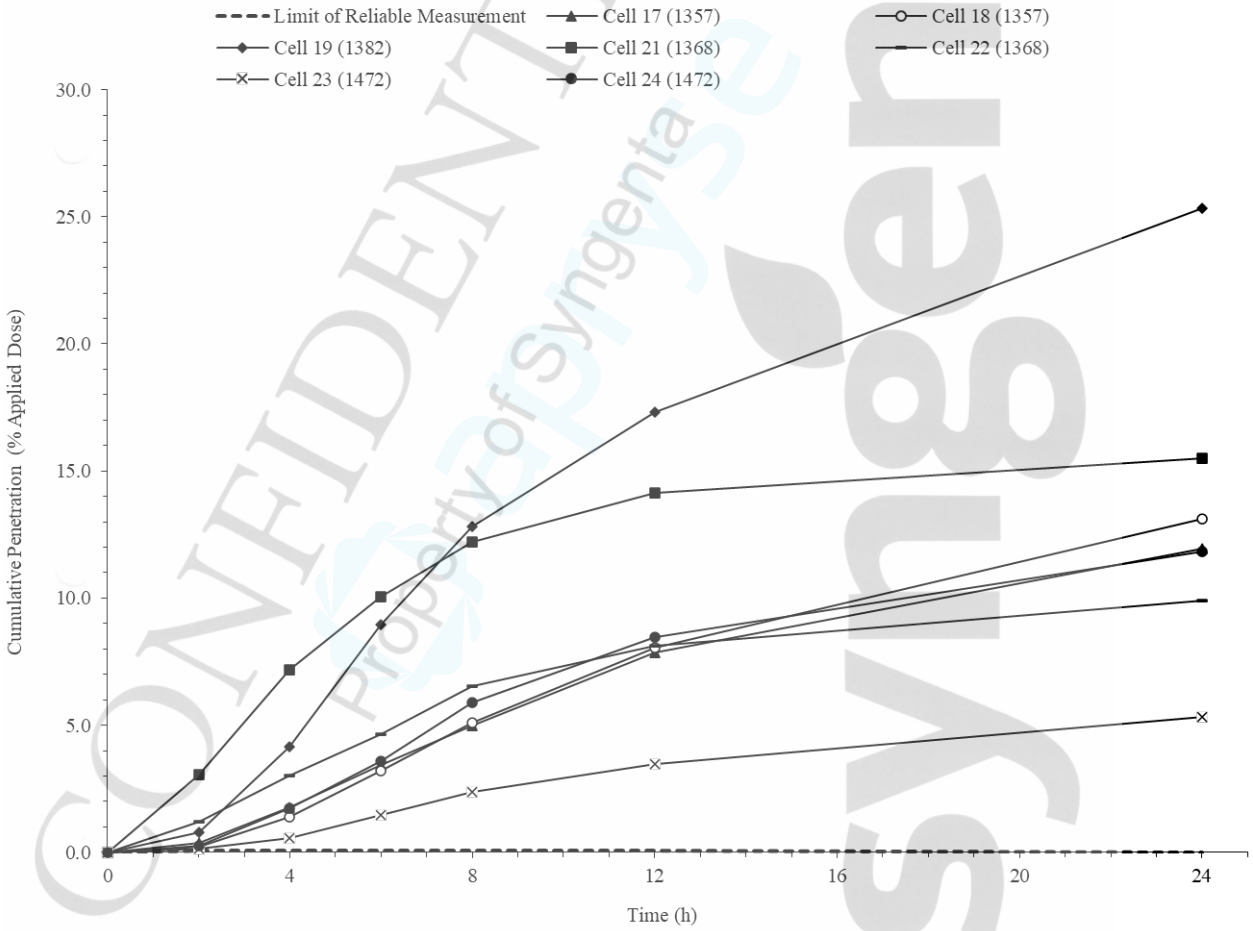


FIGURE 13 **Absorption Profile for [^{14}C]-Propiconazole (% Applied Dose) in Receptor Fluid Following Topical Application of [^{14}C]-Propiconazole in Spray Dilution 2 (0.625 g/L) to Human Split-Thickness Membranes (Mean + SD, n = 7)**

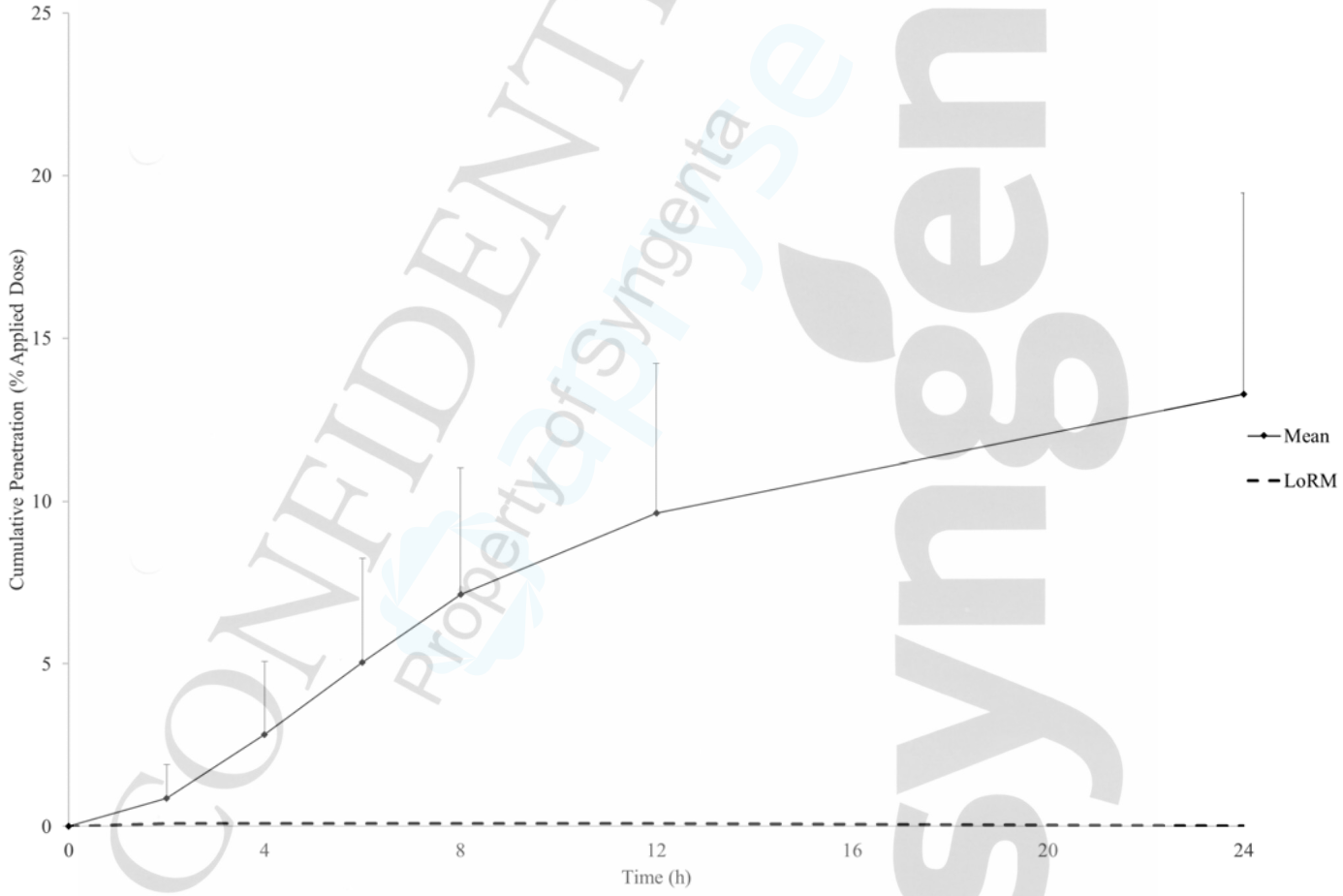


FIGURE 14 **Absorption Profile for [^{14}C]-Propiconazole (µg equiv./cm^2) in Receptor Fluid Following Topical Application of [^{14}C]-Propiconazole in Spray Dilution 2 (0.625 g/L) to Human Split-Thickness Membranes (Mean + SD, n = 7)**

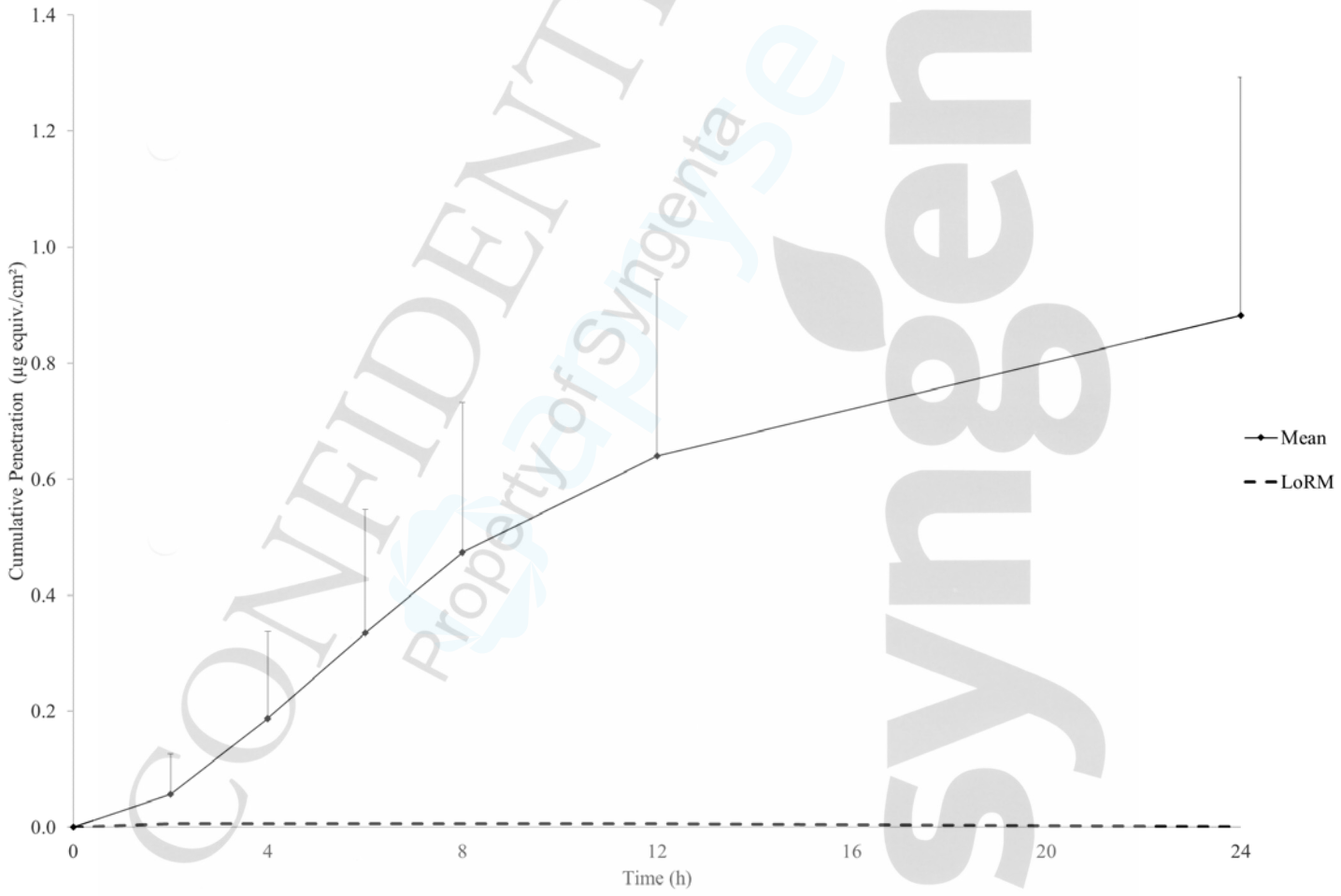


FIGURE 15 **Distribution of [^{14}C]-Propiconazole (µg equiv./cm^2) in the *Stratum Corneum* at 24 h Post Dose Following Topical Application of [^{14}C]-Propiconazole in Spray Dilution 2 (0.625 g/L) to Human Split-Thickness Membranes (Mean + SD, n = 7)**

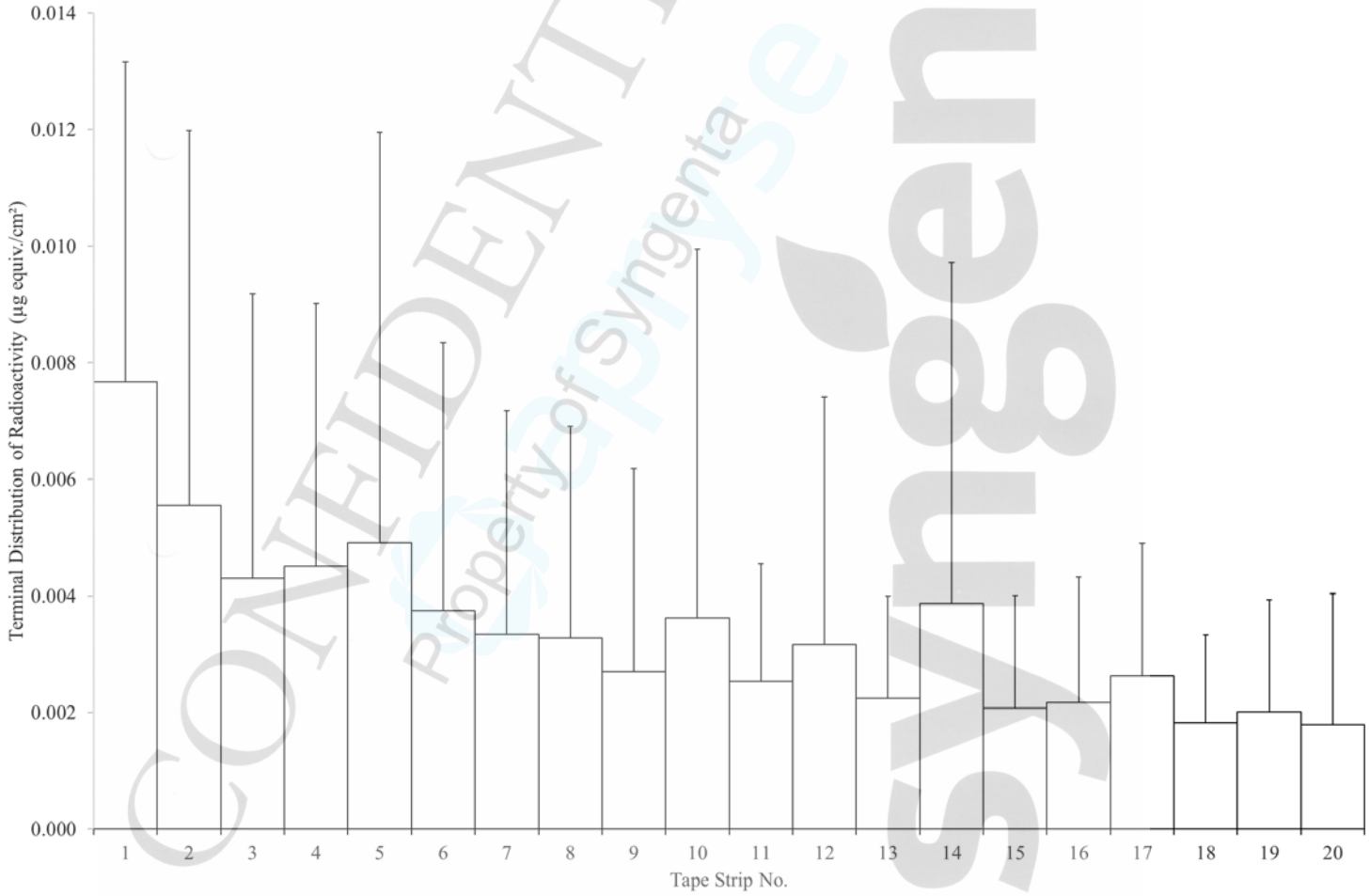


FIGURE 16 **Individual Absorption Profiles for [^{14}C]-Fenpropidin (% Applied Dose) in Receptor Fluid Following Topical Application of [^{14}C]-Fenpropidin in Formulation Concentrate (275 g/L) to Human Split-Thickness Membranes**

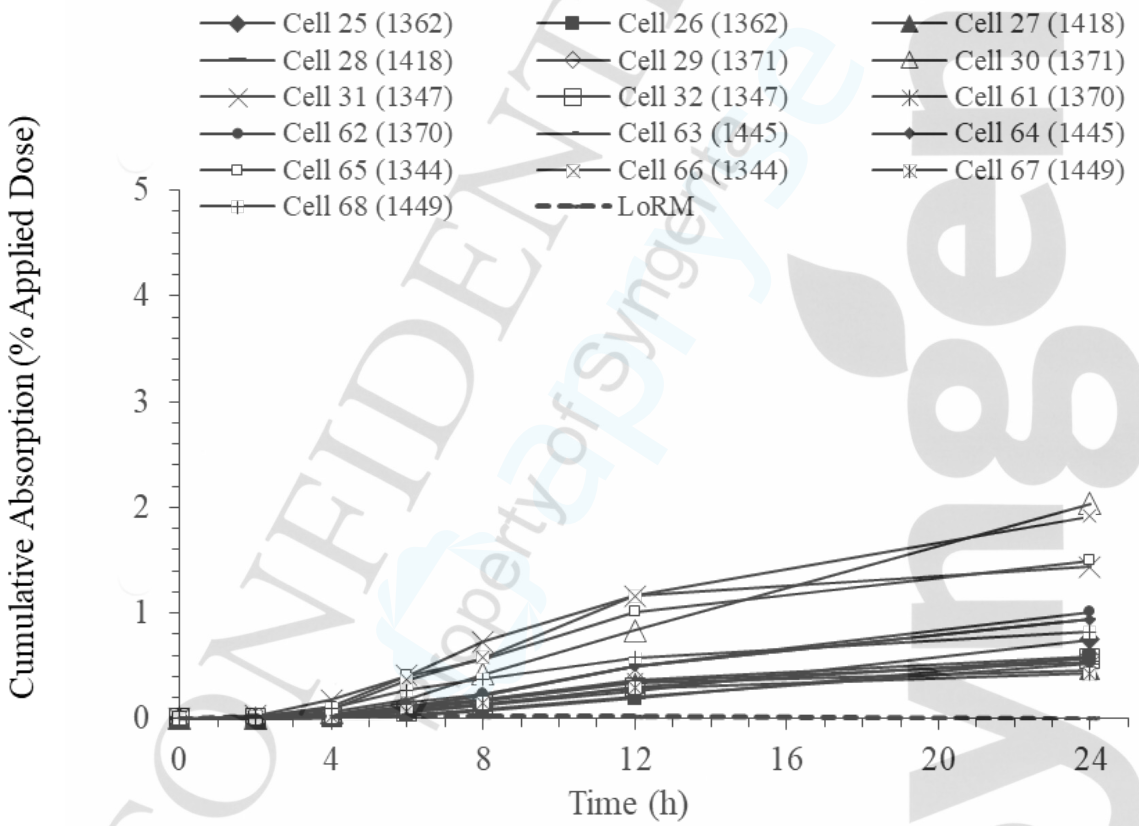


FIGURE 17 **Individual Absorption Profiles for [^{14}C]-Fenpropidin (% Applied Dose) in Receptor Fluid Following Topical Application of [^{14}C]-Fenpropidin in Formulation Concentrate (275 g/L) to Human Split-Thickness Membranes (Excluding Cells 27 and 32)**

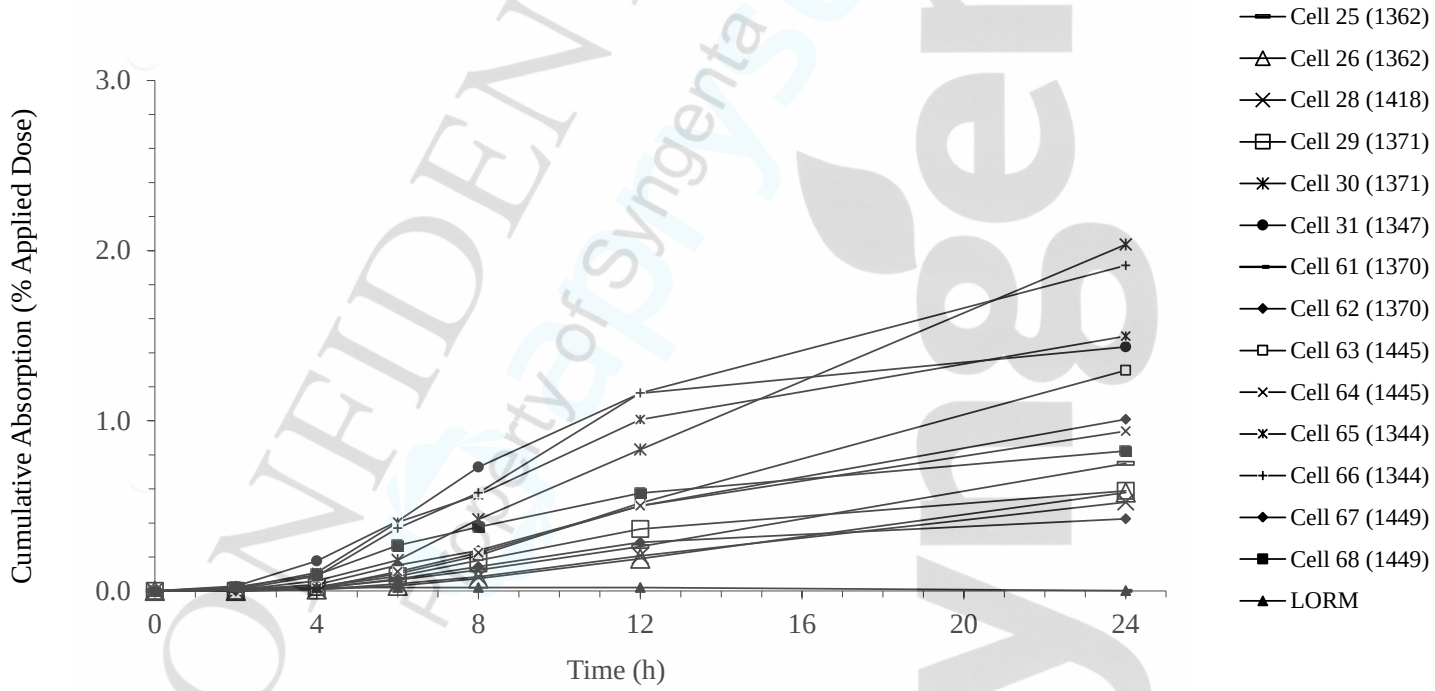


FIGURE 18 **Absorption Profile for [^{14}C]-Fenpropidin (% Applied Dose) in Receptor Fluid Following Topical Application of [^{14}C]-Fenpropidin in Formulation Concentrate (275 g/L) to Human Split-Thickness Membranes (Mean + SD, n = 14)**

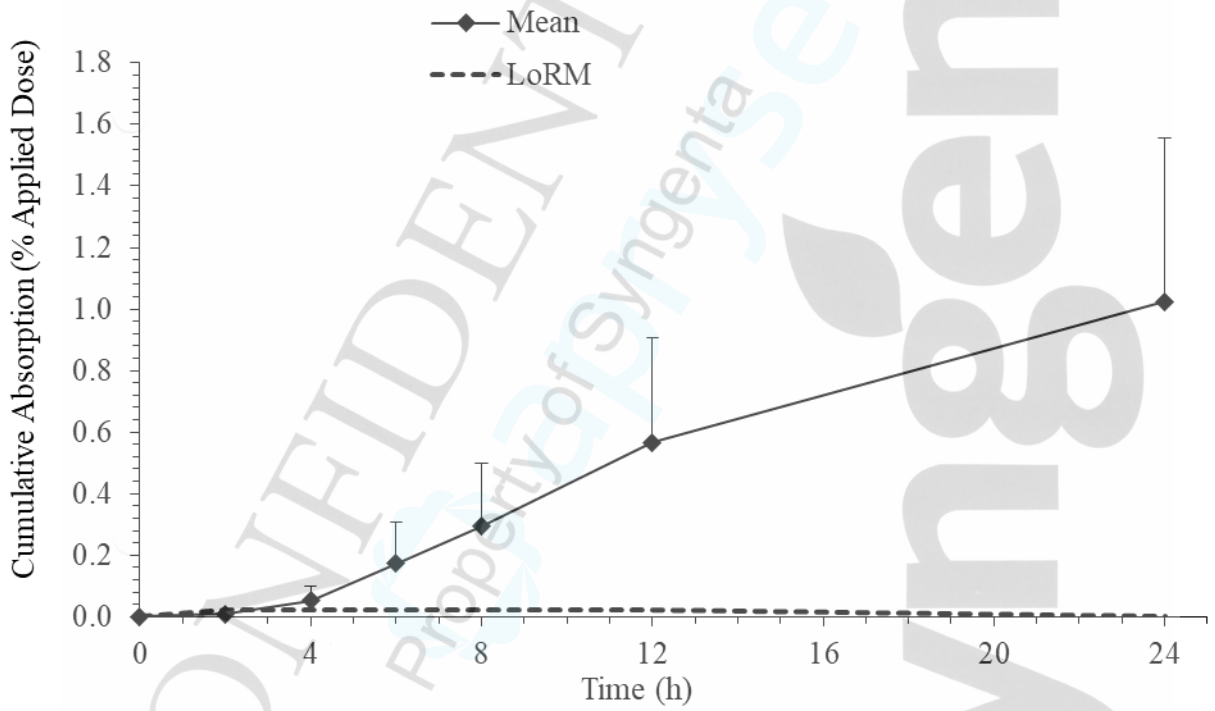


FIGURE 19 **Absorption Profile for [^{14}C]-Fenpropidin (µg equiv./cm^2) in Receptor Fluid Following Topical Application of [^{14}C]-Fenpropidin in Formulation Concentrate (275 g/L) to Human Split-Thickness Membranes (Mean + SD, n = 14)**

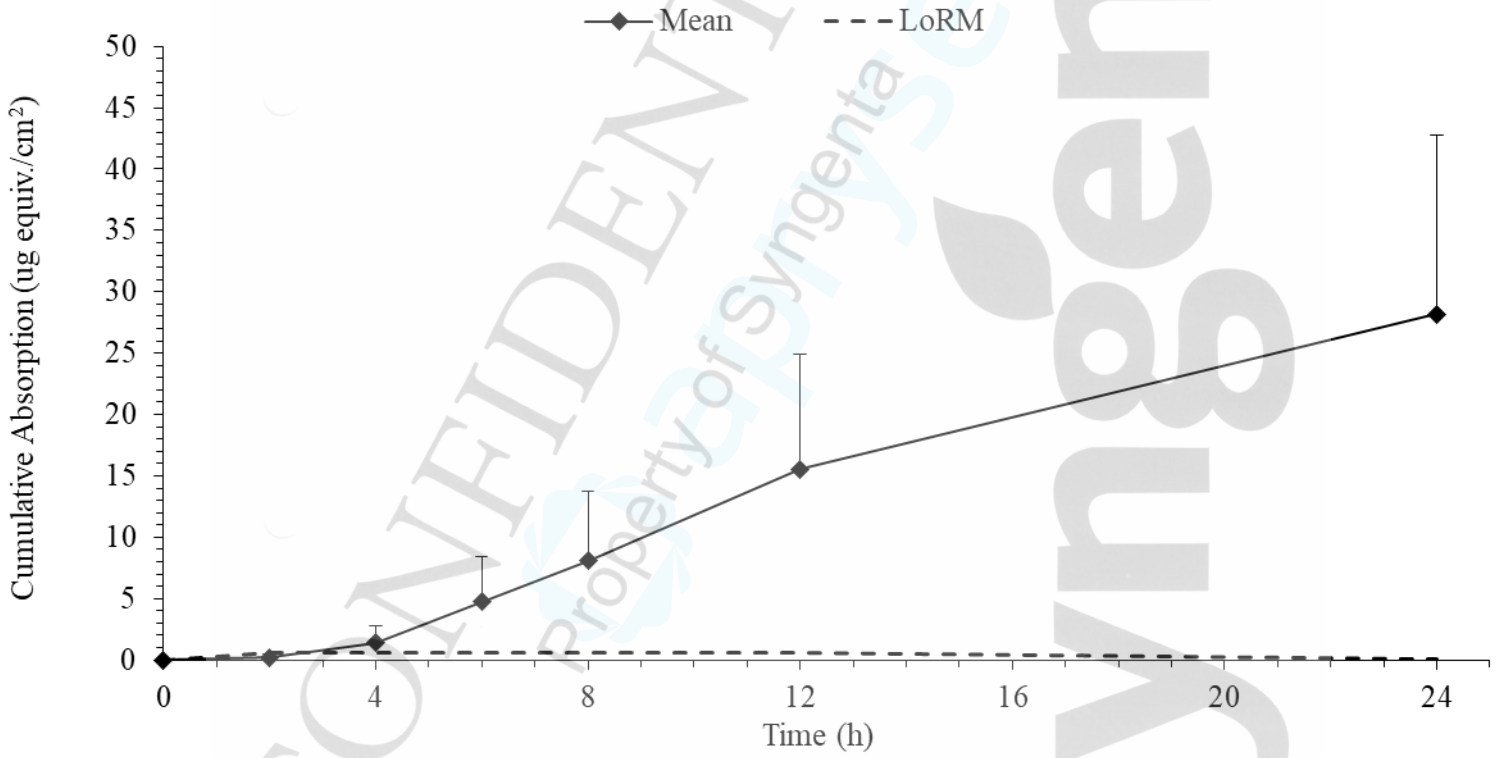


FIGURE 20 **Distribution of [^{14}C]-Fenpropidin (µg equiv./cm^2) in the *Stratum Corneum* at 24 h Post Dose Following Topical Application of [^{14}C]-Fenpropidin in Formulation Concentrate (275 g/L) to Human Split-Thickness Membranes (Mean + SD, n = 14)**

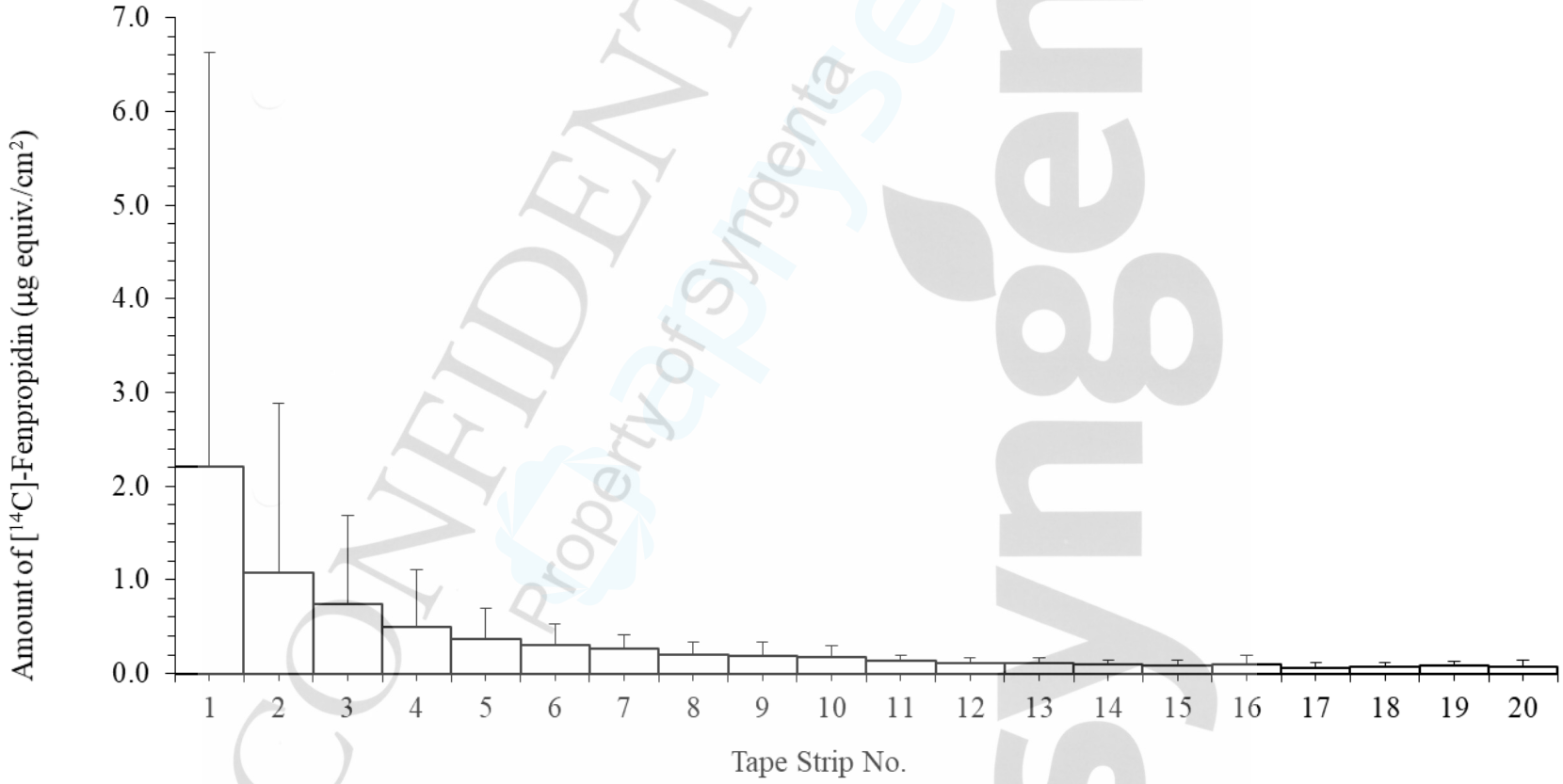


FIGURE 21 **Individual Absorption Profiles for [^{14}C]-Fenpropidin (% Applied Dose) in Receptor Fluid Following Topical Application of [^{14}C]-Fenpropidin in Spray Dilution 1 (13.75 g/L) to Human Split-Thickness Membranes**

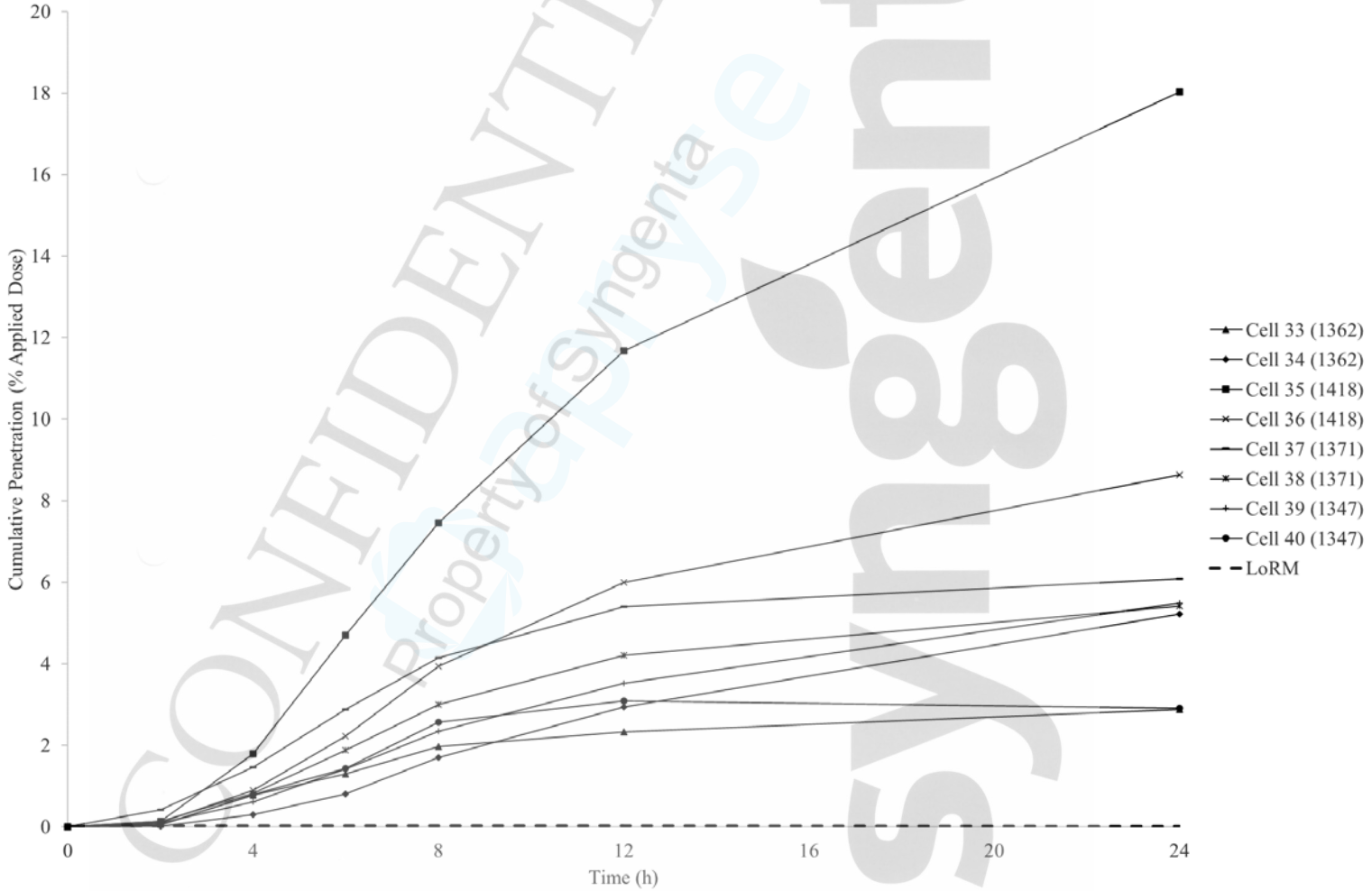


FIGURE 22 **Absorption Profile for [^{14}C]-Fenpropidin (% Applied Dose) in Receptor Fluid Following Topical Application of [^{14}C]-Fenpropidin in Spray Dilution 1 (13.75 g/L) to Human Split-Thickness Membranes (Mean + SD, n = 8)**

FIGURE 23 **Absorption Profile for [^{14}C]-Fenpropidin (µg equiv./cm^2) in Receptor Fluid Following Topical Application of [^{14}C]-Fenpropidin in Spray Dilution 1 (13.75 g/L) to Human Split-Thickness Membranes (Mean + SD, n = 8)**

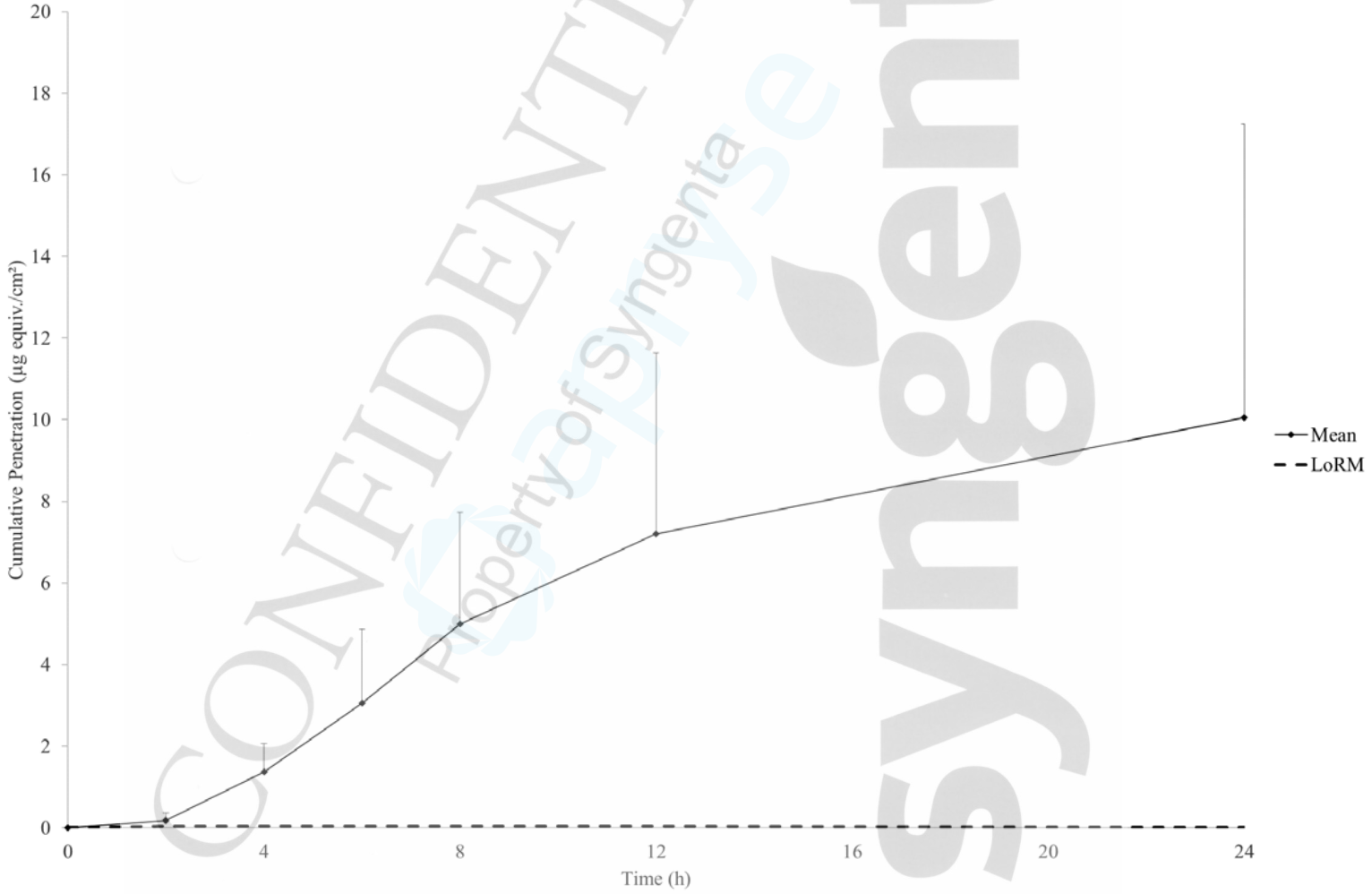


FIGURE 24 **Distribution of [^{14}C]-Fenpropidin (µg equiv./cm^2) in the *Stratum Corneum* at 24 h Post Dose Following Topical Application of [^{14}C]-Fenpropidin in Spray Dilution 1 (13.75 g/L) to Human Split-Thickness Membranes (Mean + SD, n = 8)**

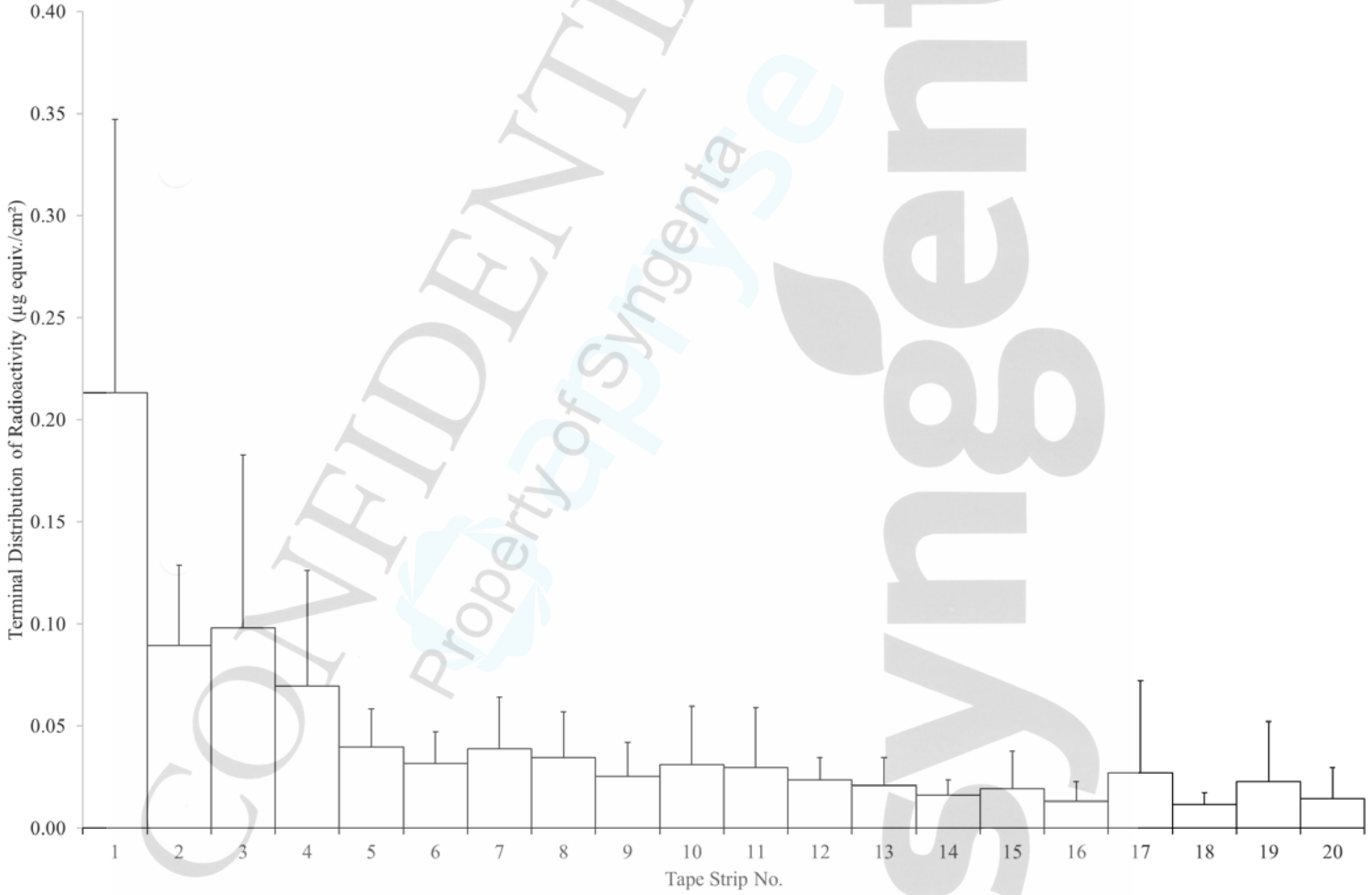


FIGURE 25 **Individual Absorption Profiles for [^{14}C]-Fenpropidin (% Applied Dose) in Receptor Fluid Following Topical Application of [^{14}C]-Fenpropidin in Spray Dilution 2 (1.375 g/L) to Human Split-Thickness Membranes**

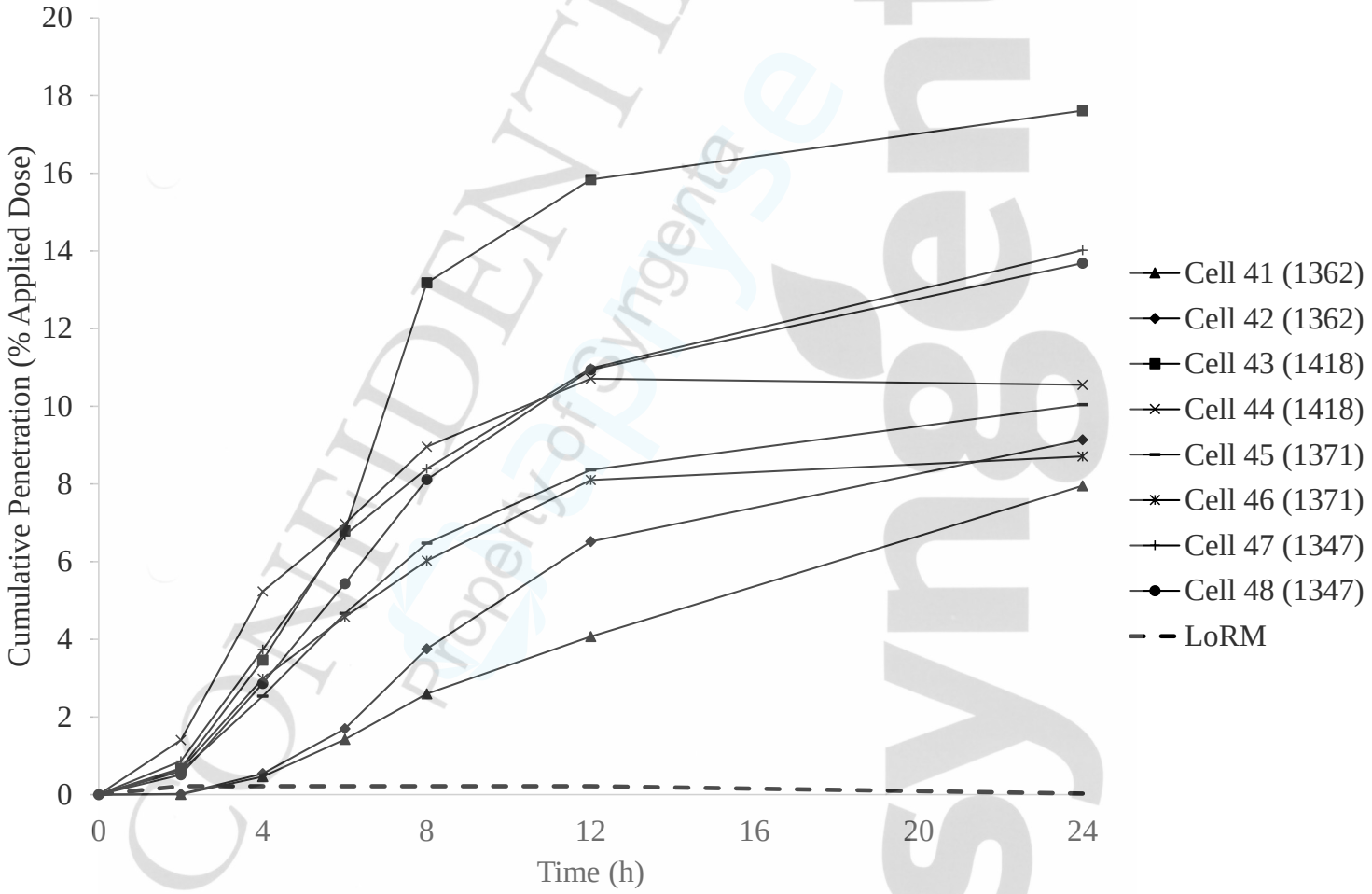


FIGURE 26 **Individual Absorption Profiles for [^{14}C]-Fenpropidin (% Applied Dose) in Receptor Fluid Following Topical Application of [^{14}C]-Fenpropidin in Spray Dilution 2 (1.375 g/L) to Human Split-Thickness Membranes (Excluding Cell 47)**

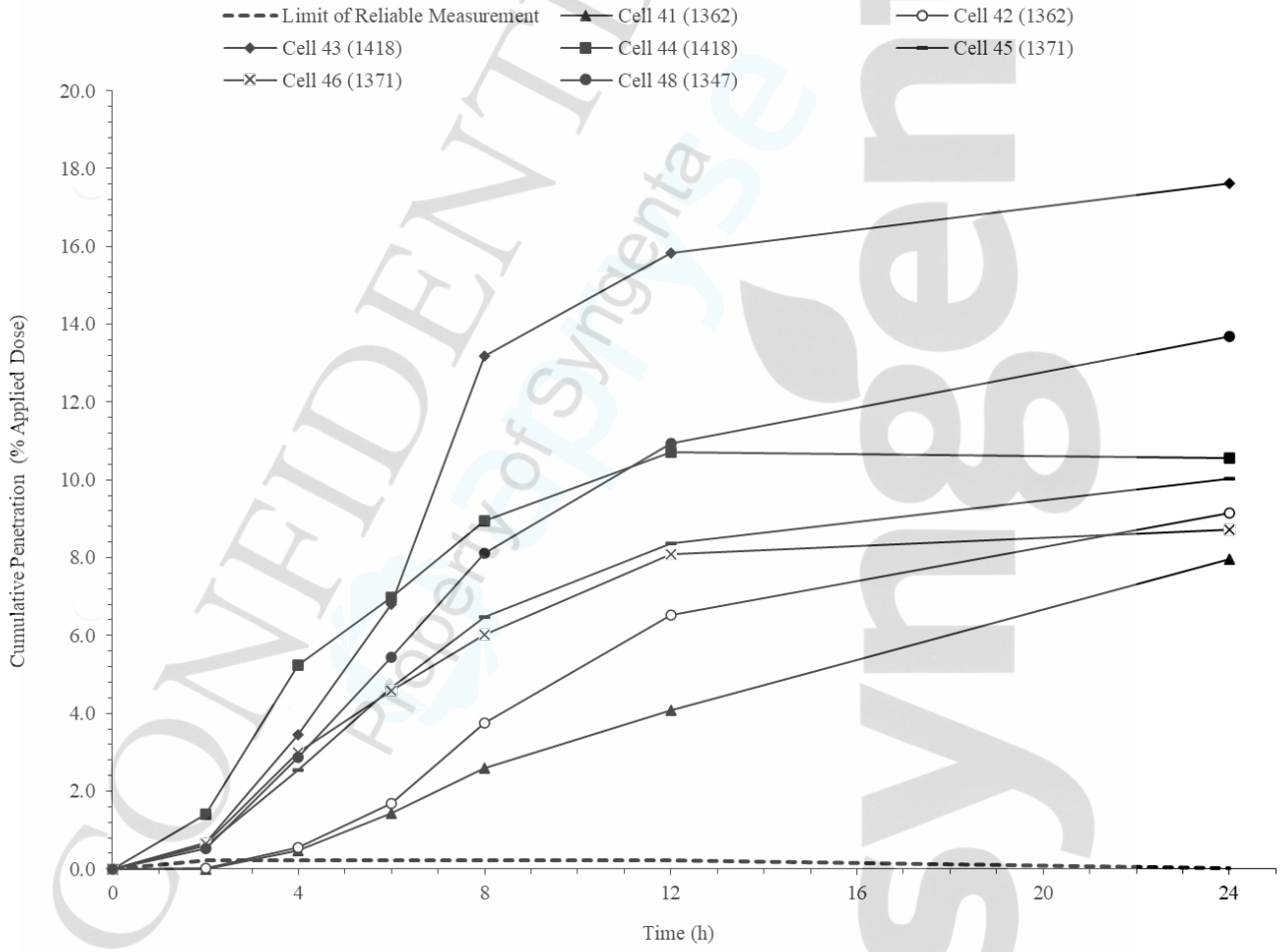


FIGURE 27 **Absorption Profile for [^{14}C]-Fenpropidin (% Applied Dose) in Receptor Fluid Following Topical Application of [^{14}C]-Fenpropidin in Spray Dilution 2 (1.375 g/L) to Human Split-Thickness Membranes (Mean + SD, n = 7)**

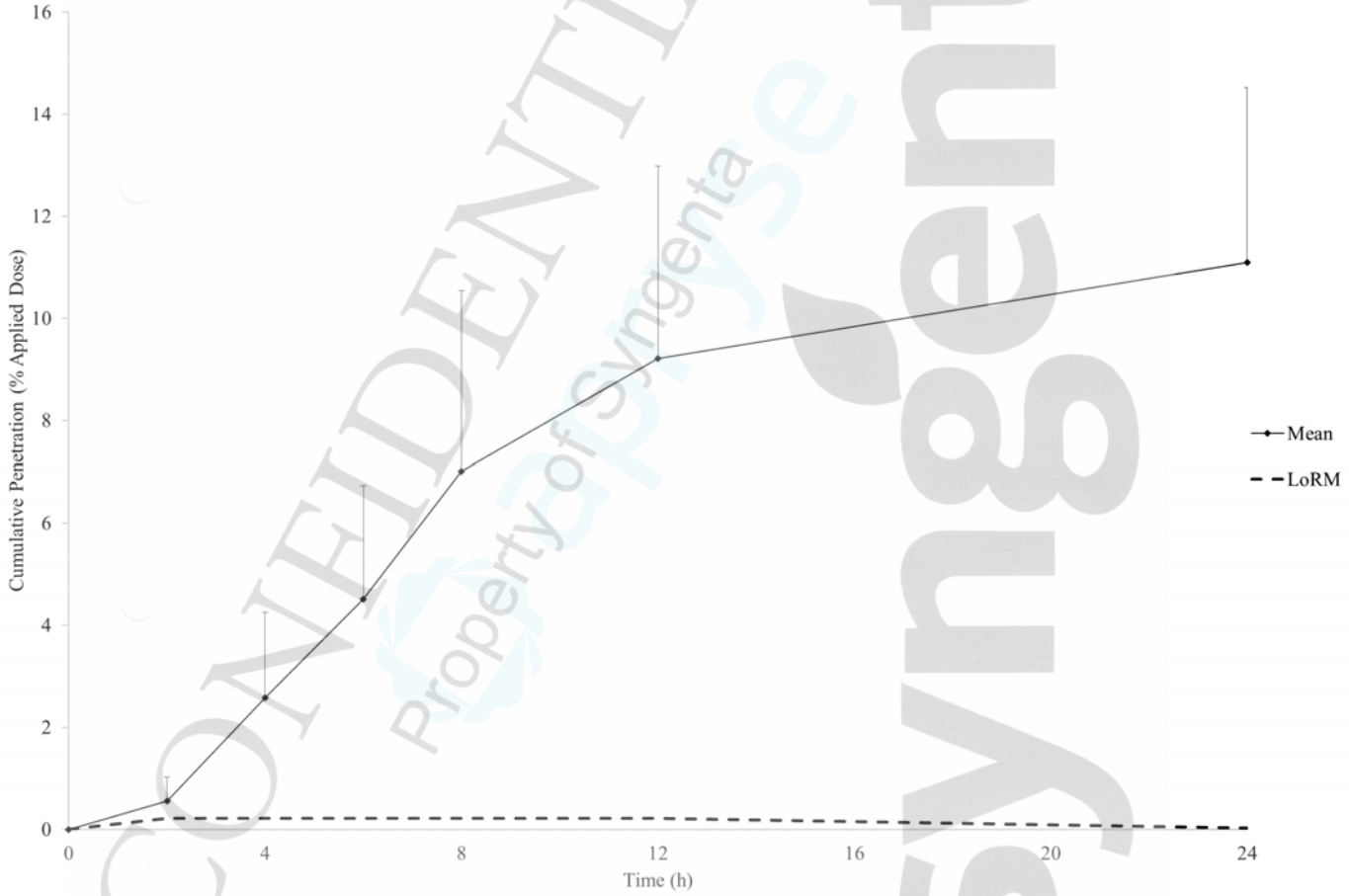


FIGURE 28 **Absorption Profile for [^{14}C]-Fenpropidin (µg equiv./cm^2) in Receptor Fluid Following Topical Application of [^{14}C]-Fenpropidin in Spray Dilution 2 (1.375 g/L) to Human Split-Thickness Membranes (Mean + SD, n = 7)**

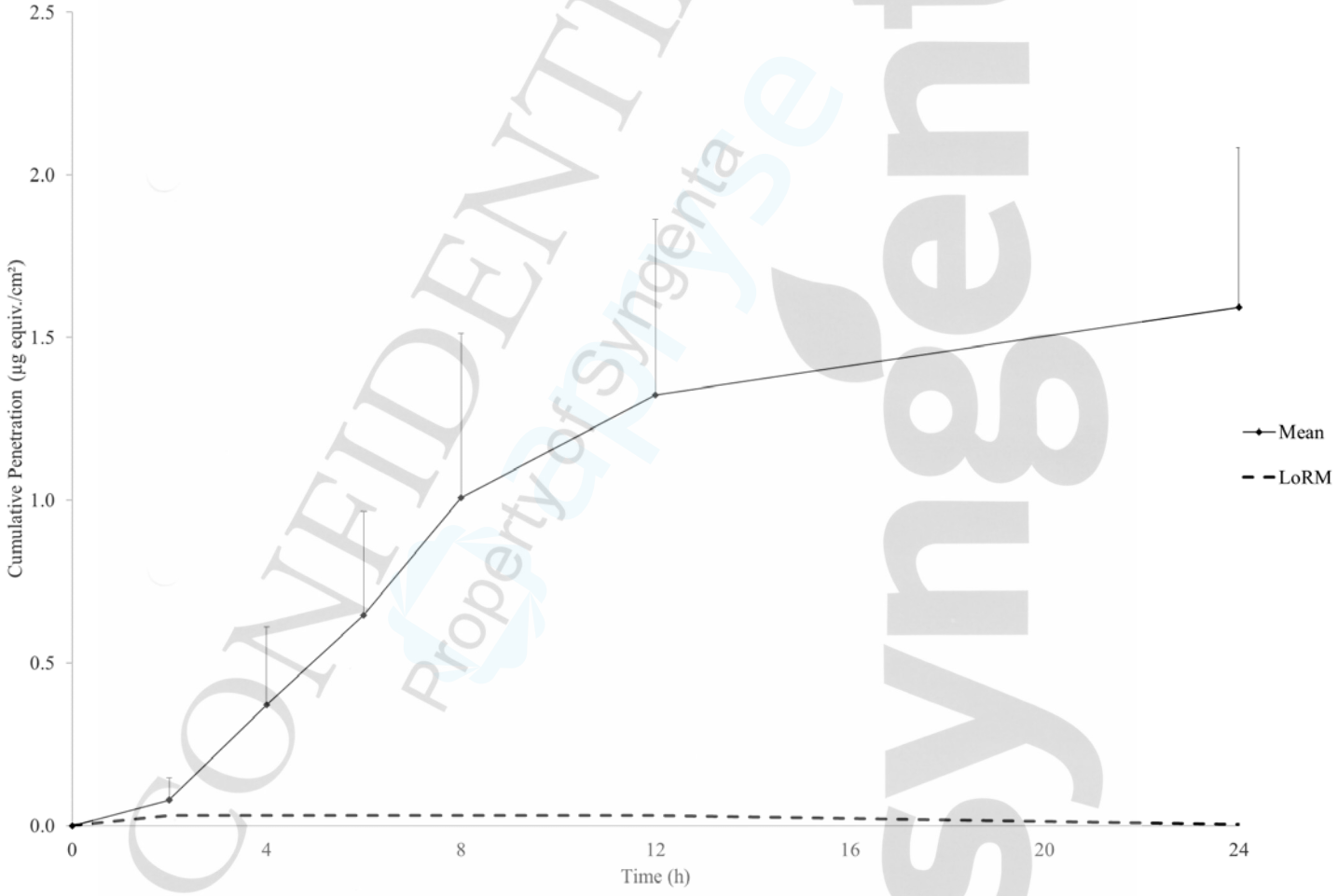
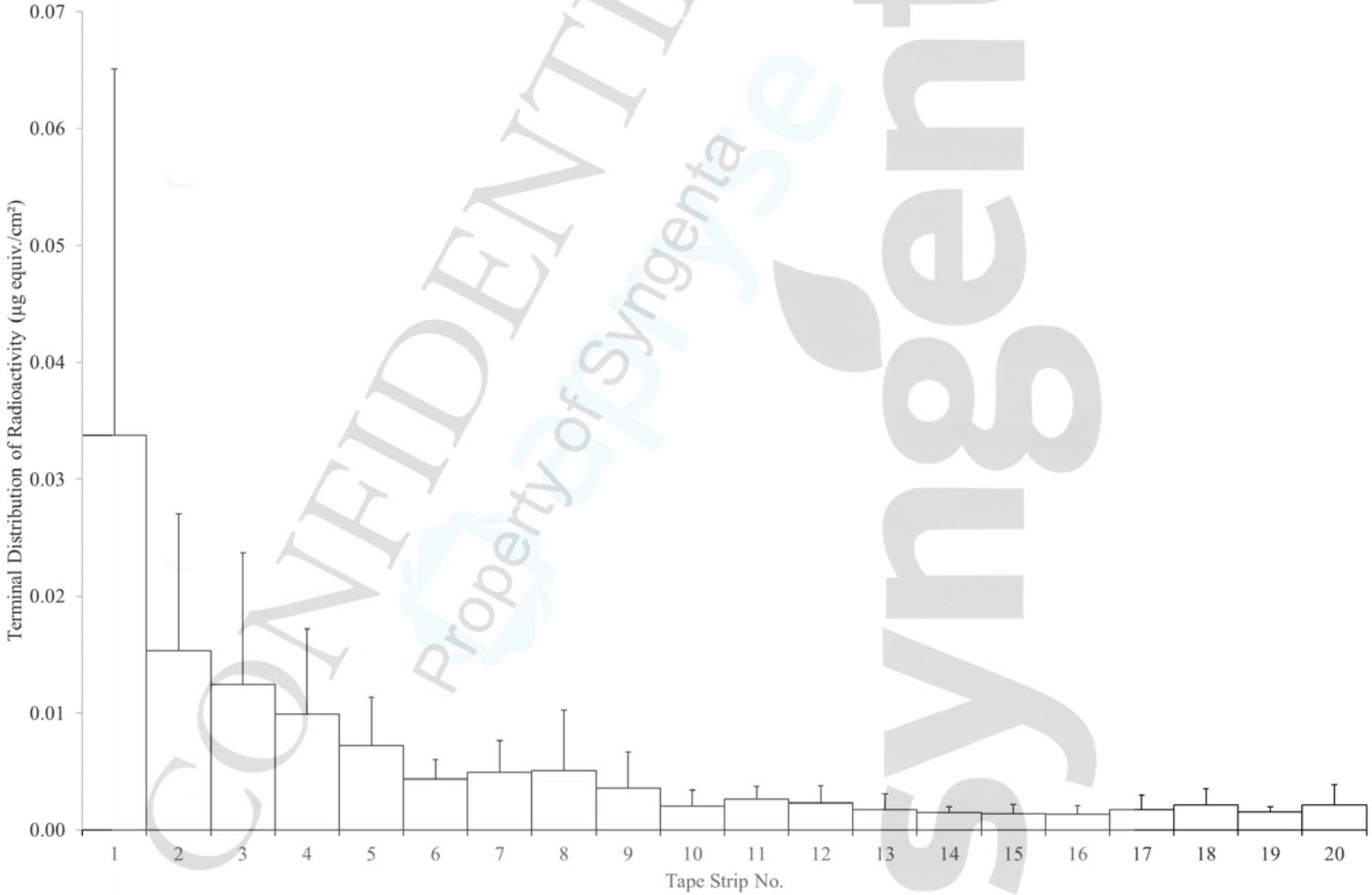


FIGURE 29 **Distribution of [^{14}C]-Fenpropidin (µg equiv./cm^2) in the *Stratum Corneum* at 24 h Post Dose Following Topical Application of [^{14}C]-Fenpropidin in Spray Dilution 2 (1.375 g/L) to Human Split-Thickness Membranes (Mean + SD, n = 7)**



APPENDICES SECTION

APPENDIX 1 GLP Certificate for Charles River

Department of Health & Social Care

THE DEPARTMENT OF HEALTH & SOCIAL CARE OF THE GOVERNMENT OF THE UNITED KINGDOM

GOOD LABORATORY PRACTICE

STATEMENT OF COMPLIANCE

TEST FACILITY	TEST TYPE(S)
CHARLES RIVER LABORATORIES EDINBURGH LIMITED ELPHINSTONE RESEARCH CENTRE TRANENT EH33 2NE UNITED KINGDOM	Analytical/Clinical Chemistry Environmental Fate Environmental Toxicity Ecosystems Physical/Chemical Testing Residue Studies Mutagenicity Toxicology

DATE OF INSPECTION: 16/03/2021 – 22/03/2021

DATE OF ISSUE: 22/11/2021

Due to COVID-19 travel restrictions, a remote inspection for compliance with the Principles of Good Laboratory Practice was carried out at the above named test facility as part of the UK Good Laboratory Practice Compliance Monitoring Programme.

This statement confirms that, on the date of issue, the UK Good Laboratory Practice Monitoring Authority were satisfied that the above named test facility was operating in compliance with the UK Good Laboratory Practice Regulations, Statutory Instrument 1999 No. 3106 (as amended) which incorporate the OECD Principles of Good Laboratory Practice.

This statement constitutes a Good Laboratory Practice Instrument as defined in the UK Good Laboratory Practice Regulations, Statutory Instrument 1999 No. 3106 (as amended).

Issued by
Mr Stephen Vinter
Head, UK GLP Monitoring Authority

Medicines & Healthcare products Regulatory Agency

MHRA

Best available copy

APPENDIX 2 Certificate of Analysis for [^{14}C]-Propiconazole

SYNGENTA CROP PROTECTION LLC
PRODUCT SAFETY NA / PRODUCT SAFETY OPERATIONS
GREENSBORO, NORTH CAROLINA, USA

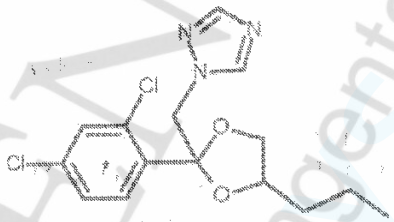
CERTIFICATE OF ANALYSIS

SYNGENTA CODE: [PHENYL-U-14C]-CGA064250

SYNONYMNS: [PHENYL-U-14C]-CSAA054101

REFERENCE NUMBER (Batch Identification): ATS-21-57212-2

STRUCTURE:



(* denotes universal ring radiolabel)

CHEMICAL PURITY: 99.7%

RADIOCHEMICAL PURITY: 98.9%

SPECIFIC ACTIVITY: 61.0 µCi/mg

STATEMENT OF GLP COMPLIANCE:

The characterization study described in this Certificate of Analysis was conducted in compliance with EPA Good Laboratory Practice Standards; U.S.A., 40 CFR Part 160, August 17, 1989. Data obtained in conjunction with this characterization study have been archived at Syngenta Crop Protection LLC, Greensboro, NC.

STORAGE CONDITIONS: Refrigerator

EXPIRATION DATE: April 30, 2022

STUDY COMPLETION DATE: November 02, 2021

STUDY DIRECTOR: Aagam Patel

SIGNATURE: Aagam Patel

CLASSIFICATION: PUBLIC

Best available copy

ANALYTICAL STANDARD
CHARACTERIZATION REPORT

IDENTITY

- COMPARISON TO AN AUTHENTIC STANDARD:
  Reference: (data ref.: R21-61/4; test date: 10/26/21)

  Thin-Layer Chromatography Systems:

  Silica gel plate; Ethyl Acetate: Cyclohexanes (3:1); Rf = 0.29
  C8 plate; Acetonitrile: Isopropanol: Water (5:2:3); Rf = 0.41

- SPECTRAL IDENTITY:

MASS SPECTROMETRY	:	Consistent with proposed structure. Reference: (data ref.: R21-61/4, MS21115; test date: 10/27/21)

PURITY

CHEMICAL PURITY – AREA DISTRIBUTION BY HPLC	:	99.7% (isomers summed) Reference: (data ref.: R21-61/1,2,3; test date: 10/26/21)
RADIOCHEMICAL PURITY – AREA DISTRIBUTION BY THIN-LAYER CHROMATOGRAPHY		98.9% (isomers summed) Reference: (data ref.: R21-61/4; test date: 10/26/21) Thin Layer Chromatography Systems: Silica gel plate; Ethyl Acetate: Cyclohexanes (3:1); Rf = 0.29 C8 plate; Acetonitrile: Isopropanol: Water (5:2:3); Rf = 0.41

SPECIFIC ACTIVITY

SPECIFIC ACTIVITY – EXTERNAL STANDARD ANALYSIS BY HPLC		61.0 µCi/mg Reference: (data ref.: R21-61/1,2,3; test date: 10/26/21)

CLASSIFICATION: PUBLIC

Best available copy

APPENDIX 3 Certificate of Analysis for [^{14}C]-Fenpropidin

SYNGENTA CROP PROTECTION LLC
NA PRODUCT SAFETY OPERATIONS
GREENSBORO, NORTH CAROLINA, USA

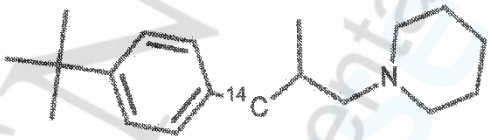
CERTIFICATE OF ANALYSIS

SYNGENTA CODE: [N-METHYLPROPYL-3-14C]-CGA114900

SYNONYMNS: [N-METHYLPROPYL-3-14C]-CSAA104478

REFERENCE NUMBER (Batch Identification): NP-21-58296-2

STRUCTURE:



CHEMICAL PURITY: 98.9%

RADIOCHEMICAL PURITY: 99.0%

SPECIFIC ACTIVITY: 199.5 µCi/mg

STATEMENT OF GLP COMPLIANCE:

The characterization study described in this Certificate of Analysis was conducted in compliance with EPA Good Laboratory Practice Standards; U.S.A., 40 CFR Part 160, August 17, 1989. Data obtained in conjunction with this characterization study have been archived at Syngenta Crop Protection LLC, Greensboro, NC.

STORAGE CONDITIONS: Freezer

EXPIRATION DATE: May 31, 2022

STUDY COMPLETION DATE: November 11, 2021

STUDY DIRECTOR: Aagam Patel

SIGNATURE: Aagam Patel

CLASSIFICATION: PUBLIC

Best available copy

ANALYTICAL STANDARD CHARACTERIZATION REPORT

IDENTITY

- **COMPARISON TO AN AUTHENTIC STANDARD:**
  Reference: (data ref.: R21-62/4,5; test date: 11/3/21)

  High Performance Liquid Chromatography System:

Column:	MicroSolv Cogent Amide Hydride 4µ (25 x 0.46 cm)
Mobile Phase:	Acetonitrile: 0.1% Aqueous Formic Acid (50:50)
Flow Rate:	1.0 ml/min
Column Temp.:	25 °C
Detection:	UV @ 225 nm (BW = 4 nm); BetaRAM with Liquid Flowcell
Run Time:	15 min.
Rt (Standard):	4.2 min.
Rt (Samples):	4.3 min.

- **SPECTRAL IDENTITY:**

MASS SPECTROMETRY	: Consistent with proposed structure. Reference: (data ref.: R21-62/6; MS21118; test date: 11/3/21)

PURITY

CHEMICAL PURITY – AREA DISTRIBUTION BY HPLC	: 98.9% Reference: (data ref.: R21-62/1,2,3; test date: 11/2/21)
RADIOCHEMICAL PURITY – AREA DISTRIBUTION BY HPLC / RAM	99.0% Reference: (data ref.: R21-62/4,5; test date: 11/3/21)
	HPLC analytical conditions are listed above for the Identity – Comparison to an Authentic Standard test.

SPECIFIC ACTIVITY

SPECIFIC ACTIVITY – EXTERNAL STANDARD ANALYSIS BY CAPILLARY HPLC	199.5 µCi/mg Reference: (data ref.: R21-62/1,2,3; test date: 11/2/21)

CLASSIFICATION: PUBLIC

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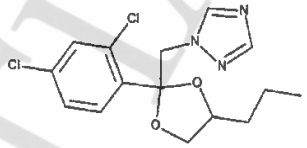
APPENDIX 4 Certificate of Analysis for Propiconazole Technical

Syngenta Crop Protection AG
GLP Testing Facility WMU
Analytical Development & Product Chemistry
Breitenloh 5
4333 Münchwilen, Switzerland

Certificate of Analysis

Propiconazole



WRS 1329/1 - Purity 96.3 %

Batch Identification	**WRS 1329/1**
Other Batch ID	571778
Product Code	**CGA64250**
Other Product Code(s)	---
ISO Common Name	propiconazole
CA Reg. No.	60207-90-1
CA Index Name	1H-1,2,4-triazole, 1-[[2-(2,4-dichlorophenyl)-4-propyl-1,3-dioxolan-2-yl]methyl]-
IUPAC Name	(+-)-1-[2-(2,4-dichlorophenyl)-4-propyl-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazole
Molecular formula	$C_{15}H_{17}Cl_2N_3O_2$
Molecular mass	342.2
Chemical Analysis	
– **Identity of Propiconazole***	**confirmed**
– **Content of Propiconazole (sum of CGA93590 and CGA93591)***	**96.3 % w/w** (estimated error: ± 0.5 %)
– **Content of CGA93590***	**54.6 % w/w**
– **Content of CGA93591***	**41.7 % w/w**
Methodology used for Characterization / Recertification	NMR, GC, IR, Karl Fischer Titration
Physical Analysis	
– **Appearance***	**brownish clear viscous liquid**
Stability:	
– **Storage Temperature**	**< 30 °C**
– **Recertification Date**	**End of September 2027**

If stored under the conditions given above, this test substance can be considered stable until the recertification date is reached.
This Certificate of Analysis summarizes data which originates either from a single study or from several individual studies. Tests marked with an asterisk (*) have been conducted in compliance with GLP.
Raw data, documentation, study plans, any amendments to study plans and reports pertaining to this/these study/studies are stored under the study number(s) referenced below within the archives of the GLP Testing Facility WMU at Syngenta Crop Protection AG, Switzerland.

Study number of batch characterization:	SMG10270
Study number(s) of batch recertification:	125651, CHMU160813, CHMU210528

Authorization: 02-Sep-2021

Urs Spuhler
Analytical Development & Product Chemistry

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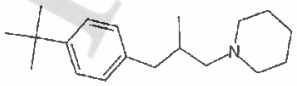
APPENDIX 5 Certificate of Analysis for Fenpropidin Technical

syngenta

Syngenta Crop Protection AG
GLP Testing Facility WMU
Analytical Development & Product Chemistry
Breitenloh 5
4333 Münchwilen, Switzerland

Certificate of Analysis

Fenpropidin tech.



UU20017829 - Purity: 100.4 %

Batch Identification	**UU20017829**
Other Batch ID	1126933
Product Code	**CGA114900 tech.**
Other Product Code(s)	CGA114900A
ISO Common Name	Fenpropidin
CA Reg. No.	67306-00-7
CA Index Name	piperidine, 1-[3-[4-(1,1-dimethylethyl)phenyl]-2-methylpropyl]-
IUPAC Name	(R,S)-1-[3-(4-tert-butylphenyl)-2-methylpropyl]-piperidine
Molecular formula	$C_{19}H_{31}N$
Molecular mass	273.5

Chemical Analysis

– **Identity of Fenpropidin***	**confirmed**
– **Content of Fenpropidin***	**100.4 % w/w**
– **Content of water***	**0.07 % w/w**
	The detailed results of the characterization are listed in the final report
Methodology used for Characterization / Recertification	GC, Karl Fischer Titration

Physical Analysis

– **Appearance***	**colorless liquid**

Stability:

– **Storage Temperature**	**< 30 °C**
– **Recertification Date**	**End of March 2023**

If stored under the conditions given above, this test substance can be considered stable until the recertification date is reached.
This Certificate of Analysis summarizes data which originates either from a single study or from several individual studies. Tests marked with an asterisk (*) have been conducted in compliance with GLP.
Raw data, documentation, study plans, any amendments to study plans and reports pertaining to this/these study/studies are stored under the study number(s) referenced below within the archives of the GLP Testing Facility WMU at Syngenta Crop Protection AG, Switzerland.

Study number of batch characterization: CHMU200273
Study number(s) of batch recertification:

Authorization: 11th March 2020

Dr. Marianthi Zampakou
Analytical Development & Product Chemistry

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APPENDIX 6 Certificate of Analysis for Commercial Formulation

Syngenta Crop Protection AG
GLP Testing Facility WMU
Analytical Development & Product Chemistry
Breitenloh 5
4333 Münchwilen, Switzerland

Certificate of Analysis

A9050B

propiconazole/fenpropidin EC (125/275)

STH001-015-001

Batch Identification	**STH001-015-001**
Other Batch ID	1162447
Product Code	**A9050B**
Other Product Code(s)	CGA64250/CGA114900 EC (125/275)
Chemical Analysis (Active Ingredient content)	
– **Identity of the Active Ingredient(s)***	**confirmed**
– **Content of propiconazole (sum of CGA93590 and CGA93591)***	**13.1 % w/w corresponding to 125 g/l**
– **Content of CGA93590***	**7.49 % w/w corresponding to 71.4 g/l**
– **Content of CGA93591***	**5.61 % w/w corresponding to 53.5 g/l**
– **Content of fenpropidin***	**28.8 % w/w corresponding to 274 g/l**
	The Active Ingredient(s) content is within the FAO limits.
Methodology used for Characterization / Recertification	GC, oscillating density meter
Physical Analysis	
– **Appearance**	**light yellow liquid**
– **Density***	**953 kg/m³**
Stability:	
– **Storage Temperature**	**< 30 °C**
– **Recertification Date**	**End of September 2025**

If stored under the conditions given above, this test substance can be considered stable until the recertification date is reached.
This Certificate of Analysis summarizes data which originates either from a single study or from several individual studies. Tests marked with an asterisk (*) have been conducted in compliance with GLP.
Raw data, documentation, study plans, any amendments to study plans and reports pertaining to this/these study/studies are stored under the study number(s) referenced below within the archives of the GLP Testing Facility WMU at Syngenta Crop Protection AG, Switzerland.

Study number of batch characterization:	CHMU200985
Study number(s) of batch recertification:	---

Authorization: 12-Nov-2020

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Analytical Development & Product Chemistry

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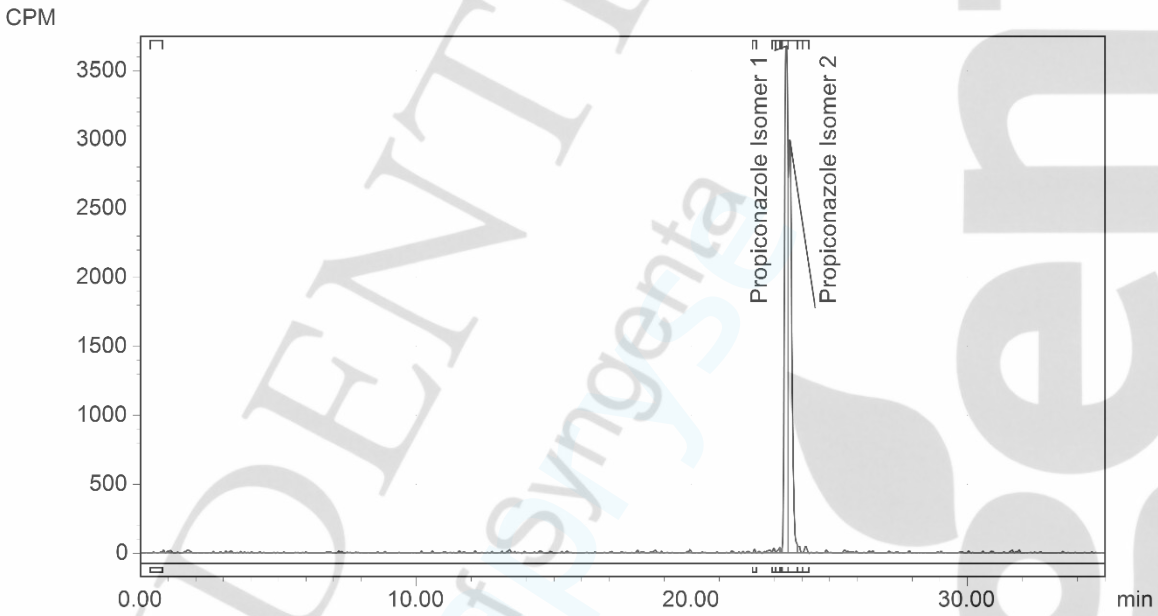
APPENDIX 7 HPLC Chromatogram for Radiochemical Purity of [^{14}C]-Propiconazole

Chromatogram: ^{14}C
Sample Name: RCP 1
File Name 788252_16Nov2021 Run 3 Eval 1.Evaluation

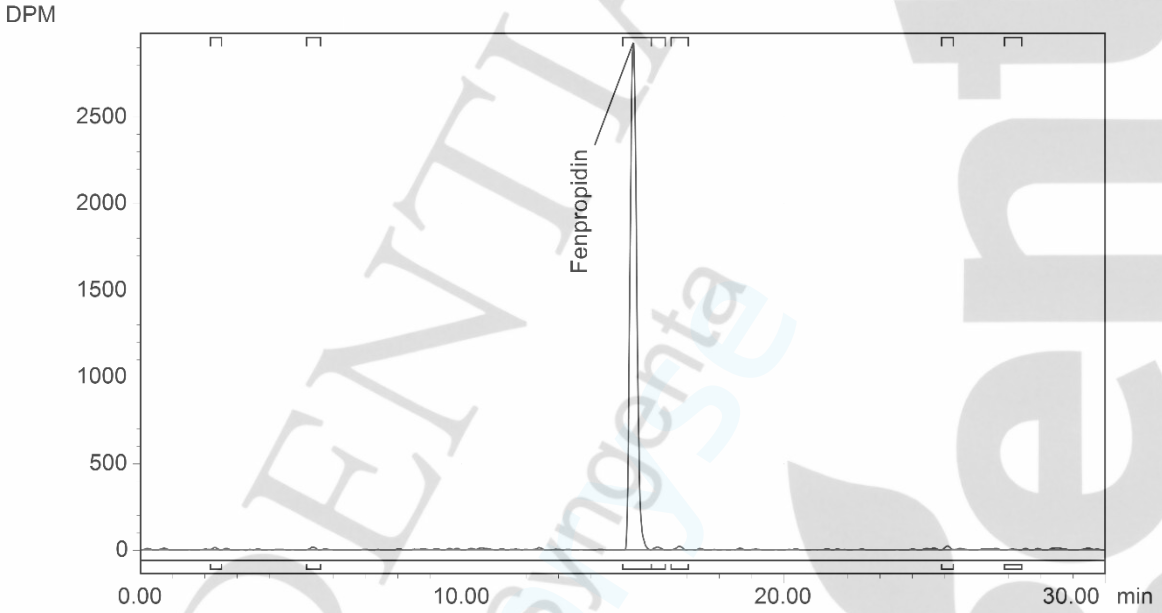


Peak Name	Retention Time (min)	%ROI (%)
-	22.27	0.2
-	22.97	0.3
-	23.17	0.3
-	23.20	0.2
-	23.25	0.1
Propiconazole Isomer 1	23.43	49.7
Propiconazole Isomer 2	23.57	48.1
-	23.88	0.6
-	24.13	0.5

The 2 peaks on the chromatogram correspond to 2 isomers of Propiconazole with purity of 49.7% and 48.1% each. The combined radiochemical purity is 97.8%

APPENDIX 8 HPLC Chromatogram for Radiochemical Purity of [^{14}C]-Fenpropidin

Chromatogram: ^{14}C
Sample Name: RCP101
File Name 788252_26Nov2021 Run 3 Eval 1.Evaluation



Peak Name	Retention Time (min)	%ROI (%)
-	2.35	0.3
-	5.38	0.4
Fenpropidin	15.32	97.8
-	16.08	0.5
-	16.80	0.6
-	25.07	0.5

APPENDIX 9 Human Skin Donor Details

Charles River Donor No.	Sex/Age	Site	Supplier
1344	F/48	Abdomen	Tissue Solutions
1347	F/45	Abdomen	Tissue Solutions
1357	F/38	Abdomen	Tissue Solutions
1362	F/32	Abdomen	Tissue Solutions
1368	F/36	Abdomen	Tissue Solutions
1370	F/53	Abdomen	Tissue Solutions
1371	F/34	Abdomen	Tissue Solutions
1382	F/56	Abdomen	Tissue Solutions
1418	F/38	Abdomen	Tissue Solutions
1445	F/35	Abdomen	Tissue Solutions
1449	F/47	Abdomen	Tissue Solutions
1472	M/49	Abdomen	Biopredic

APPENDIX 10 Thickness of Full and Split-Thickness Skin Membranes

Charles River Donor No.	Membrane Thickness (µm)	
	Full Thickness Skin	Split-Thickness Skin
1344	1250	400
1347	1050-1400	360-400
1357	970-1190	390-400
1362	1000-1100	350-390
1368	1490-1950	390-400
1370	1050	390
1371	1100-1220	340-390
1382	870-1400	400
1418	1430-1810	380-400
1445	1110	400
1449	1400	400
1472	1790-2110	400

APPENDIX 11 Cross Reference of Cell Number with Donor Number and Electrical Resistance

Cell Number	Charles River Donor No.	Electrical Resistance (kΩ)
1	1357	8.778
2	1357	10.64
3	1382	8.765
4	1382	8.988
5	1368	10.24
6	1368	14.64
7	1472	17.86
8	1472	16.65
9	1357	10.03
10	1357	7.819
11	1382	10.52
12	1382	10.71
13	1368	10.74
14	1368	11.76
15	1472	15.00
16	1472	14.72
17	1357	9.204
18	1357	9.313
19	1382	9.787
20	1382	10.51
21	1368	13.14
22	1368	11.42
23	1472	17.13
24	1472	10.37
25	1362	11.12
26	1362	10.35
27	1418	8.605
28	1418	12.51
29	1371	14.97
30	1371	11.46
31	1347	10.95
32	1347	13.44
33	1362	14.97
34	1362	10.41
35	1418	7.970
36	1418	7.901
37	1371	7.957
38	1371	14.80
39	1347	12.19

Cell Number	Charles River Donor No.	Electrical Resistance (kΩ)
40	1347	11.53
41	1362	11.50
42	1362	9.860
43	1418	7.851
44	1418	12.35
45	1371	12.13
46	1371	8.402
47	1347	11.93
48	1347	11.67
61	1370	23.45
62	1370	22.98
63	1445	8.278
64	1445	8.225
65	1344	11.60
66	1344	9.216
67	1449	10.01
68	1449	8.645
69	1370	16.50
70	1370	13.34
71	1445	9.335
72	1445	9.167
73	1344	8.031
74	1344	8.285
75	1449	10.35
76	1449	9.713
77	1370	12.11
78	1370	12.11
79	1445	7.948
80	1445	9.646
81	1344	15.40
82	1344	10.02
83	1449	11.84
84	1449	14.89

Rejection criterion: sample rejected if electrical resistance <7.7 kΩ for split-thickness skin.

After the initial set up of the split-thickness skin membranes in the diffusion cell system, electrical resistance measurements were taken. Where the resistance was <7.7 kΩ (*i.e.* the acceptance criterion was not met), the skin was replaced with a new piece and the electrical resistance re-measured. Details for all failed skin samples, which were subsequently replaced, are provided in the table below. Details for the final measurements for all samples which passed are provided in the table above.

Cell Number	Charles River Donor No.	Electrical Resistance (kΩ)
18	1357	6.973
29	1371	6.339
46	1371	4.960
37	1371	6.884
37 (1st repeat)	1371	6.498

APPENDIX 12 Epidermis Removal by Tape Stripping

The *stratum corneum* was removed with successive tape strips. Where epidermis was removed, this is detailed in the table below. The value for this tape strip has been added to the exposed skin value.

Cell Number	Tape Strip Number (Fraction of Epidermis Removed)
27	SC10 (3/4)
27	SC13 (Trace)
27	SC14 (Trace)
29	SC18 (3/4)
30	SC6 (3/4)
35	SC6 (1/8)
37	SC20 (1/4)
38	SC1 (Trace)
38	SC14 (1/4)
38	SC19 (Full)
43	SC6 (Trace)
46	SC18 (1/4)
65	SC19 (1/4)
66	SC18 (Trace)
75	SC6 (1/5)
81	SC19 (Trace)

APPENDIX 13 Limit of Reliable Measurement in Each Matrix (% Applied Dose and µg equiv./cm^2)

[^{14}C]-Propiconazole

Formulation Concentrate

Occasion 1

	Limit of Reliable Measurement	
Sample Type	%	µg equiv./cm^2
Receptor Fluid 0 h	0	0
Receptor Fluid 2-12 h	0.0240	0.305
Receptor Fluid 24 h	0.00288	0.0366
Skin Wash	0.00575	0.0733
Tissue Swabs¥	0.00144	0.0183
Pipette Tips	0.00144	0.0183
Donor Wash	0.00719	0.0916
Receptor Wash	0.0115	0.147
Stratum Corneum	0.00144	0.0183
Unexposed Skin	0.00144	0.0183
Exposed Skin	0.00144	0.0183

Occasion 2

	Limit of Reliable Measurement	
Sample Type	%	µg equiv./cm^2
Receptor Fluid 0 h	0	0
Receptor Fluid 2-12 h	0.0230	0.293
Receptor Fluid 24 h	0.00276	0.0351
Skin Wash	0.00551	0.0703
Tissue Swabs¥	0.00138	0.0176
Pipette Tips	0.00138	0.0176
Donor Wash	0.00689	0.0879
Receptor Wash	0.0110	0.141
Stratum Corneum	0.00138	0.0176
Unexposed Skin	0.00138	0.0176
Exposed Skin	0.00138	0.0176

Spray Dilution 1

Occasion 1

	Limit of Reliable Measurement	
Sample Type	%	µg equiv./cm^2
Receptor Fluid 0 h	0	0
Receptor Fluid 2-12 h	0.00888	0.00577
Receptor Fluid 24 h	0.00106	0.000692
Skin Wash	0.00213	0.00138
Tissue Swabs¥	0.000532	0.000346
Pipette Tips	0.000532	0.000346
Donor Wash	0.00266	0.00173
Receptor Wash	0.00426	0.00277
Stratum Corneum	0.000532	0.000346
Unexposed Skin	0.000532	0.000346
Exposed Skin	0.000532	0.000346

Occasion 2

	Limit of Reliable Measurement	
Sample Type	%	µg equiv./cm^2
Receptor Fluid 0 h	0	0
Receptor Fluid 2-12 h	0.00972	0.005770
Receptor Fluid 24 h	0.00117	0.000692
Skin Wash	0.00233	0.00139
Tissue Swabs¥	0.000583	0.000346
Pipette Tips	0.000583	0.000346
Donor Wash	0.00292	0.00173
Receptor Wash	0.00466	0.00277
Stratum Corneum	0.000583	0.000346
Unexposed Skin	0.000583	0.000346
Exposed Skin	0.000583	0.000346

Spray Dilution 2

	Limit of Reliable Measurement	
Sample Type	%	µg equiv./cm2
Receptor Fluid 0 h	0	0
Receptor Fluid 2-12 h	0.0869	0.00577
Receptor Fluid 24 h	0.0104	0.000692
Skin Wash	0.0208	0.00139
Tissue Swabs¥	0.00521	0.000346
Pipette Tips	0.00521	0.000346
Donor Wash	0.0261	0.00173
Receptor Wash	0.0417	0.00277
Stratum Corneum	0.00521	0.000346
Unexposed Skin	0.00521	0.000346
Exposed Skin	0.00521	0.000346

[^{14}C]-Fenpropidin

Formulation Concentrate

Occasion 1

	Limit of Reliable Measurement	
Sample Type	%	µg equiv./cm^2
Receptor Fluid 0 h	0	0
Receptor Fluid 2-12 h	0.0200	0.550
Receptor Fluid 24 h	0.00240	0.0660
Skin Wash	0.00480	0.132
Tissue Swabs¥	0.00120	0.0330
Pipette Tips	0.00120	0.0330
Donor Wash	0.0480	1.32
Receptor Wash	0.00961	0.264
Stratum Corneum	0.00120	0.0330
Unexposed Skin	0.00120	0.0330
Exposed Skin	0.00120	0.0330

Occasion 2

	Limit of Reliable Measurement	
Sample Type	%	µg equiv./cm^2
Receptor Fluid 0 h	0	0
Receptor Fluid 2-12 h	0.0212	0.582
Receptor Fluid 24 h	0.00254	0.0699
Skin Wash	0.00508	0.140
Tissue Swabs¥	0.00127	0.0349
Pipette Tips	0.00127	0.0349
Donor Wash	0.0508	1.40
Receptor Wash	0.0102	0.280
Stratum Corneum	0.00127	0.0349
Unexposed Skin	0.00127	0.0349
Exposed Skin	0.00127	0.0349

Spray Dilution 1

	Limit of Reliable Measurement	
Sample Type	%	µg equiv./cm^2
Receptor Fluid 0 h	0	0
Receptor Fluid 2-12 h	0.0211	0.0311
Receptor Fluid 24 h	0.00254	0.00373
Skin Wash	0.00507	0.00747
Tissue Swabs	0.00127	0.00187
Pipette Tips	0.00127	0.00187
Filters	0.0761	0.112
Donor Wash	0.0507	0.0747
Receptor Wash	0.0101	0.0149
Stratum Corneum	0.00127	0.00187
Unexposed Skin	0.00127	0.00187
Exposed Skin	0.00127	0.00187

Spray Dilution 2

	Limit of Reliable Measurement	
Sample Type	%	µg equiv./cm^2
Receptor Fluid 0 h	0	0
Receptor Fluid 2-12 h	0.217	0.0311
Receptor Fluid 24 h	0.0260	0.00373
Skin Wash	0.0520	0.00747
Tissue Swabs	0.0130	0.00187
Pipette Tips	0.0130	0.00187
Filters	0.780	0.112
Donor Wash	0.520	0.0747
Receptor Wash	0.104	0.0149
Stratum Corneum	0.0130	0.00187
Unexposed Skin	0.0130	0.00187
Exposed Skin	0.0130	0.00187

¥: This is the value for each individual tissue swab sample. At 24 h post dose a single sample was analysed, at 6 h post dose the 5 swabs were analysed individually so the value will be 5 times this for the overall 6 h tissue swab sample.

APPENDIX 14 OECD Guidelines Glossary of Terms

GLOSSARY OF TERMS

Absorbed dose (*in vivo*): comprises that present in urine, cage wash, faeces, expired air (if measured), blood, tissues (if collected) and the remaining carcass, following removal of application site skin.

Absorbed dose (*in vitro*): mass of test substance reaching the receptor fluid or systemic circulation within a specified period of time.

Absorbable dose (*in vitro and in vivo*) represents that present on or in the skin following washing.

Absorption (Dermal, Percutaneous and Skin absorption): diffusion of chemicals from the outer surface of the skin to the receptor fluid or systemic circulation.

Absorption profile: a graphical representation of cumulative absorption as a function of time.

Absorption rate: mass of test substance passing through a unit area of skin into the receptor fluid or systemic circulation, per unit time (in $\mu g/cm^2/h$).

Adsorption: reversible binding or adherence the test substance to any component of the test system.

Applied dose: mass of test preparation containing a specified mass of test substance applied per cm^2 of skin.

Dermal delivery: sum of the applied dose found in the treated skin and the absorbed dose at the end of the experiment.

Dislodgeable dose: mass of test substance that is removable from the application site.

Exposure period: time from application of test preparation to removal at skin washing.

Finite dose: amount of test preparation applied to the skin where a maximum absorption rate of the test substance may be achieved for a certain time interval but is not maintained.

Flux: mass of test substance passing through a unit area of skin per unit of time under steady-state conditions (in $\mu g/cm^2/h$).

'in-use' preparation: the preparation of test substance which relates directly to potential human exposure (e.g. cosmetic or agrochemical formulations and dilutions thereof, a mixture of industrial chemicals in a solvent, etc.).

Infinite dose: amount of test preparation applied to the skin where a maximum absorption rate of the test substance is achieved and maintained.

Lag time: derived from a graph of cumulative absorbed dose and time. Intercept of the tangent of the linear part of the absorption profile with the x-axis.

Penetration enhancer: adjuvant, which facilitates penetration of the test substance through skin.

Percentage absorption: the mass of test substance absorbed (over a given time period) divided by the mass of test substance applied multiplied by 100.

Permeability coefficient (Kp): a value, in units of cm/h, that represents the rate at which a chemical penetrates the skin. This is calculated from the flux divided by the applied concentration.

Steady-state: the part of an absorption profile where the absorption rate remains constant.

Test substance: a single chemical entity whose penetration characteristics are under investigation.

Test preparation: actual material that is applied to the skin. Usually the test preparation will be the 'in-use' preparation that reflects actual use conditions; alternatively it may be a mixture of the test substance in a carrier or solvent to facilitate application to the skin.

Unabsorbed dose: represents that washed from the skin surface after exposure and any present on the non-occlusive cover, including any dose shown to volatilise from the skin during exposure.