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Cyproconazole/Isopyrazam
Cyproconazole/Isopyrazam SC (A19022A) - The *In Vitro* Percutaneous Absorption of Radiolabelled Cyproconazole and Radiolabelled Isopyrazam in Concentrate Formulation and Two In-Use Dilutions Through Human Split-thickness Skin

Final Report

DATA REQUIREMENT(S): OECD (2004) 428

AUTHOR(S): Frank Toner BSc MSB
Karolina Gruszka BSc
Leanne Page BSc

STUDY COMPLETION DATE: 26 April 2013

PERFORMING LABORATORY: Charles River
Tranent, Edinburgh
EH33 2NE, United Kingdom

LABORATORY PROJECT ID: Report Number: 34003
Study Number: 792932
Task Number: TK0147791

SPONSOR(S): Syngenta Ltd
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STATEMENT OF DATA CONFIDENTIALITY CLAIMS

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GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

Study Number: 792932
Sponsors Ref. TK0147791

Study Title: The *In Vitro* Percutaneous Absorption of Radiolabelled Cyproconazole and Radiolabelled Isopyrazam in Concentrate Formulation and Two In-Use Dilutions Through Human Split-thickness Skin.

Test Item: Cyproconazole/Isopyrazam SC (A19022A)

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 Community, United States of America (FDA and EPA) and Japan (MHLW, MAFF and METI).

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

Frank Toner — 26 April 2013

Frank Toner BSc MSB
Study Director

Date

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QUALITY ASSURANCE STATEMENT

Study Title: The *In Vitro* Percutaneous Absorption of Radiolabelled Cyproconazole and Radiolabelled Isopyrazam in Concentrate Formulation and Two In-Use Dilutions Through Human Split-thickness Skin.

The Charles River Quality Assurance Unit conducted a protocol review, study-based inspections and report audits on this study, as detailed below.

Date(s) of QA Activity	Activity	Date of Report to Management and Study Director
18 January 2013	Protocol Review	18 January 2013
24 January 2013	Dose Administration	28 January 2013
24 - 28 January 2013	Dose Preparation Review	28 January 2013
25 February - 08 March 2013	Draft Report Audit	08 March 2013
25 April 2013	Final Report Audit	25 April 2013

Process-based inspections relevant to this study are scheduled once every quarter. The outcome of each inspection is reported to Management and, where relevant, the Study Director.

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.

Jane P Dunnie — 26 April 2013

Jane Dunsire CBiol MSB
Quality Assurance

Date

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GENERAL INFORMATION

Contributors

The following contributed to this report in the capacities indicated:

Name	Title
Frank Toner BSc MSB	Study Director
Gary Wicksted BSc	Analyst
Jill Runciman HND MSB	Analyst
David McGregor	Analyst
Linda Allan BSc	Analyst
Adele Swanson BSc MSc	Analyst
Karolina Gruszka BSc	Analyst/ Report Author
Jo Vinall BSc MSc	Analyst
Claire Haldane BSc MSc	Analyst
Leanne Page BSc	Analyst
Mike Swift MSc PhD MRSC	Analyst
Susan Craig BSc	Analyst
Brijesh Goswami BSc MSc	Analyst
Alison McNaughton HNC	QA Auditor
Jane Dunsire CBiol MSB	QA Auditor
Eric Yau	Syngenta Study Manager

Study Dates

Study Initiation Date:	16 January 2013
Experimental Start Date:	16 January 2013
Experimental Completion Date:	08 February 2013

Deviations from the Guidelines

None.

Retention of Samples

All samples will be discarded following completion of the study.

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Performing Laboratory Test Substance Reference Number

Cyproconazole Technical (SAN619A) Dispense No. 120756
Isopyrazam Technical (SYN520453A) Dispense No. 120898

SYN 520453[pyrazolyl-5-14C] (CSCD602770[pyrazolyl-5-14-C] Dispense No. 130005
SAN 619F-[triazolyl -U-14C] Dispense No. 130004

A19022A blank formulation (EXF1508A) Dispense No. 120845

Other

All raw data generated and recorded during this study, including specimens will be stored in the Scientific Archive of Charles River, Preclinical Services Edinburgh for 2 years after the issue of the final report. After the 2 year period the Sponsor will be consulted regarding the disposal, transfer or continued storage of the raw data and specimens.

A reserve sample of the test item from each batch used in the study, including a sample of the reference item will be retained in the Scientific Archive of Charles River, Preclinical Services Edinburgh for a period of at least 2 years or until the quality of the material no longer affords evaluation.

The original signed copy of the final report will be stored indefinitely in the Scientific Archive of Charles River, Preclinical Services Edinburgh.

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1.0 EXECUTIVE SUMMARY

1.1 Study Design

The absorption of Cyproconazole and Isopyrazam as a suspension concentrate (SC) formulation in Cyproconazole/Isopyrazam SC (A19022A) was measured *in vitro* through human split-thickness skin. The concentration of Cyproconazole and Isopyrazam in the concentrate SC formulation was 80 g/L and 125 g/L, respectively. The highest concentration in-use spray dilution was *ca* 0.8 g/L for Cyproconazole and *ca* 1.25 g/L for Isopyrazam. The lowest concentration in-use spray dilution was *ca* 0.20 g/L for Cyproconazole and *ca* 0.31 g/L for Isopyrazam.

The doses were applied at 10 µL/cm^2 and left unoccluded 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: ethanol (1:1, v/v)) at recorded intervals throughout the experimental period. The distribution of Cyproconazole and Isopyrazam within the test system and a 24 h absorption profile were determined, using liquid scintillation counting.

1.2 Results

1.2.1 [^{14}C]-Cyproconazole formulation concentrate (Test Preparation 1, 80 g/L)

The mean absorption rate of Cyproconazole from the Formulation Concentrate 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 1.81 µg equiv./cm^2 (0.22% of the applied dose).

Following the skin wash at 6 h, 99.98% of the applied dose of Cyproconazole was washed off, with 0.58% removed with a skin wash at 24 h post dose. A proportion of the dose applied was recovered from the donor chamber (0.03%), 0.04% was found in the exposed skin and 0.01% was recovered from the receptor chamber wash. The mean total recovery was 100.88% of the applied dose.

1.2.2 [^{14}C]-Cyproconazole spray dilution 1 (Test Preparation 2, 0.8 g/L)

The mean absorption rate of Cyproconazole from Spray Dilution 1 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 1.00 µg equiv./cm^2 (11.88% of the applied dose).

Following the skin wash at 6 h, 85.63% of the applied dose of Cyproconazole was washed off, with 2.48% removed with a skin wash at 24 h post dose. A proportion of the dose applied was recovered from the donor chamber (0.05%), 0.50% was found in the exposed

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skin and 0.23% was recovered from the receptor chamber wash. The mean total recovery was 101.05% of the applied dose.

1.2.3 [^{14}C]-Cyproconazole spray dilution 2 (Test Preparation 3, 0.2 g/L)

The mean absorption rate of Cyproconazole from Spray Dilution 2 through human split-thickness skin was 0.02 µg equiv./cm^2/h during the 24 h experimental period. The amount penetrated at 24 h, as measured in the receptor fluid, was 0.47 µg equiv./cm^2 (22.05% of the applied dose).

Following the skin wash at 6 h, 73.97% of the applied dose of Cyproconazole was washed off, with 2.37% removed with a skin wash at 24 h post dose. A proportion of the dose applied was recovered from the donor chamber (0.04%), 0.50% was found in the exposed skin and 0.62% was recovered from the receptor chamber wash. The mean total recovery was 99.95% of the applied dose.

1.2.4 [^{14}C]-Isopyrazam formulation concentrate (Test Preparation 4, 125 g/L)

The mean absorption rate of Isopyrazam from formulation concentrate through human split-thickness skin was 0.01 µg equiv./cm^2/h during the 24 h experimental period. The amount penetrated at 24 h, as measured in the receptor fluid, was 0.33 µg equiv./cm^2 (0.03% of the applied dose).

Following the skin wash at 6 h, 96.11% of the applied dose of Isopyrazam was washed off, with 0.20% removed with a skin wash at 24 h post dose. A proportion of the dose applied was recovered from the donor chamber (0.01%), 0.04% was found in the exposed skin and <0.01% was recovered from the receptor chamber wash. The mean total recovery was 96.45% of the applied dose.

1.2.5 [^{14}C]-Isopyrazam spray dilution 1 (Test Preparation 5, 1.25 g/L)

The mean absorption rate of Isopyrazam from Spray Dilution 1 through human split-thickness skin was 0.01 µg equiv./cm^2/h during the 24 h experimental period. The amount penetrated at 24 h, as measured in the receptor fluid, was 0.23 µg equiv./cm^2 (1.72% of the applied dose).

Following the skin wash at 6 h, 85.58% of the applied dose of Isopyrazam was washed off, with 7.26% removed with a skin wash at 24 h post dose. A proportion of the dose applied was recovered from the donor chamber (0.10%), 1.94% was found in the exposed skin and 0.04% was recovered from the receptor chamber wash. The mean total recovery was 98.71% of the applied dose.

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1.2.6 [^{14}C]-Isopyrazam spray dilution 2 (Test Preparation 6, 0.31 g/L)

The mean absorption rate of Isopyrazam from Spray Dilution 2 through human split-thickness skin was <0.01 µg equiv./cm^2/h during the 24 h experimental period. The amount penetrated at 24 h, as measured in the receptor fluid, was 0.07 µg equiv./cm^2 (2.25% of the applied dose).

Following the skin wash at 6 h, 85.16% of the applied dose of Isopyrazam was washed off, with 8.11% removed with a skin wash at 24 h post dose. A proportion of the dose applied was recovered from the donor chamber (0.10%), 1.73% was found in the exposed skin and 0.07% was recovered from the receptor chamber wash. The mean total recovery was 99.36% of the applied dose.

1.3 Conclusion

The study demonstrated that the amount of Cyproconazole absorbed through human split-thickness skin membranes over 24 h (following a 6 h exposure) from the concentrate formulation (80 g/L), and the intended in-use concentrations, 0.8 g/L and 0.2 g/L, in Cyproconazole/Isopyrazam SC (A19022A) was 0.23%, 12.11% and 22.68% of the applied dose, respectively, as measured in the receptor fluid and receptor chamber wash.

The amount of Isopyrazam absorbed from the concentrate formulation (125 g/L), and the intended in-use concentrations, 1.25 g/L and 0.31 g/L, in Cyproconazole/Isopyrazam SC (A19022A) was 0.03%, 1.76% and 2.32% of the applied dose, respectively, as measured in the receptor fluid and receptor chamber wash.

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2.0 INTRODUCTION

2.1 Purpose

The purpose of this study was to determine the rate and extent of *in vitro* percutaneous absorption of Cyproconazole and Isopyrazam 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 Cyproconazole/Isopyrazam SC (A19022A).

The two active ingredients (Cyproconazole and Isopyrazam) will be assessed separately with the following applications:

- A 80 g Cyproconazole/L formulation concentrate (also containing Isopyrazam) and two aqueous spray strength dilutions (Spray Dilution 1 (0.8 g/L) and Spray Dilution 2 (0.2 g/L)).
- A 125 g Isopyrazam/L formulation concentrate (also containing Cyproconazole) and two aqueous spray strength dilutions (Spray Dilution 1 (1.25 g/L) and Spray Dilution 2 (0.31 g/L).

2.2 Regulatory Guidelines and Guidance Documents

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. The study was conducted according to Charles River Protocol No. 792932 and 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).

Scientific Opinion on Dermal Absorption (EFSA Journal, 2012, 10(4): 2665).

2.3 Justification and Selection of the Test System

Split-thickness human skin is an accepted system for determining dermal absorption across human skin *in vitro* and its reliability has been demonstrated at Charles River (Charles River Report No. 32053, 2011).

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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

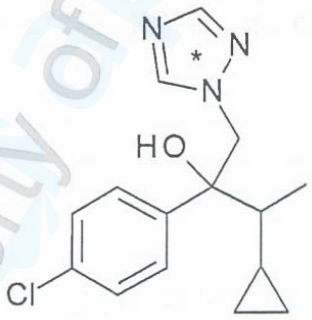
3.1 Test and Control Substances

3.1.1 Radiolabelled test item ([^{14}C]-Cyproconazole)

Name:	[Triazolyl-U-^{14}C]-Cyproconazole; SAN 619F-[triazolyl-U-14C]
Batch Number:	CDC-XXXIV-66-1
Chemical Purity:	99.4%
Radiochemical Purity:	99.3%
Specific Activity:	57.3 µCi/mg
Recommended Storage Conditions:	In the dark at +4°C
Expiry Date:	31 May 2013
Analytical Certificate Reference:	Dated: 28 November 2012

A copy of the Certificate of Analysis is presented in Appendix 1.

The structure and site of labelling (*) of [^{14}C]-Cyproconazole are shown below.



3.1.2 Radiolabelled test item ([^{14}C]-Isopyrazam)

Name:	[pyrazolyl-5-^{14}C]-Isopyrazam; SYN 520453[pyrazolyl-5-^{14}C]
Batch Number:	CDC-XXXIV-56-1
Chemical Purity:	99.5%
Radiochemical Purity:	98.2%
Specific Activity:	63.3 µCi/mg
Recommended Storage Conditions:	In the dark at +4°C
Expiry Date:	31 May 2013
Analytical Certificate Reference:	Dated: 09 November 2012

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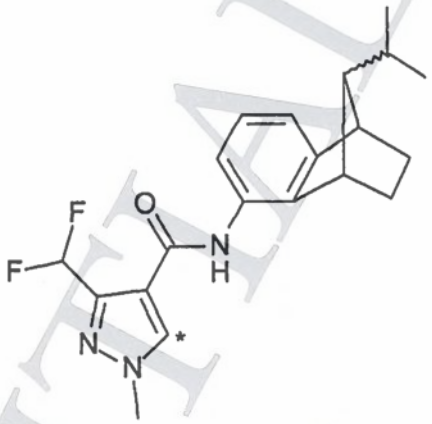
A copy of the Certificate of Analysis is presented in Appendix 2.

The structure and site of labelling (*) of [^{14}C]-Isopyrazam are shown below.



3.1.3 Non-radiolabelled test items

Name:	Cyproconazole Technical
Product Design Code:	SAN619A
Batch Number:	612042
Analytical Certificate Reference:	Dated 23 February 2011
Physical Appearance:	White powder
Purity:	98.3%
Storage Conditions:	Ambient/dark
Recertification Date:	31 January 2014

Name:	Isopyrazam Technical
Product Design Code:	SYN520453
Batch Number:	SMO0A037/1
Analytical Certificate Reference:	Dated 26 November 2010
Physical Appearance:	Off-white powder
Purity:	97.1%
Storage Conditions:	Ambient/dark
Reanalysis Date:	30 November 2014

An archive sample has been retained at Charles River. A copy of the Certificates of Analysis is presented in Appendix 3.

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3.1.4 Commercial formulation

Name:	Cyproconazole/Isopyrazam SC (A19022A)
Synonyms:	SAN619/SYN520453 SC (080/125)
Product (Design) Code:	A19022A
Batch (Lot) Number:	J8657/147
Physical Appearance:	Beige liquid
Density:	1.073 g/cm^3
Storage Conditions:	Ambient/dark
Recertification Date:	31 October 2013

3.1.5 Blank formulation

Name:	Blank of A19022A EXF1508A
Product Design Code:	EXF1508A
Batch (Lot) Number:	CCR001-013-001
Physical Appearance:	Grey greenish liquid
Density:	0.9630 g/cm^3
Storage Conditions:	Ambient/protected from light and humidity
Recertification Date:	05 November 2014

An archive sample and a copy of the Manufacturing Protocol were retained at Charles River.

3.1.6 CIPAC standard water D

CIPAC Standard Water D (batch no. 11286761) used for in-use spray dilutions was supplied by the Sponsor and stored at ambient temperature in the dark at Charles River. An archive sample was retained at Charles River.

3.1.7 Other materials

Sigma-Aldrich Company Ltd supplied the following chemicals:

- Phosphate Buffered Saline
- Minimum Essential Medium Eagle (MEME)
- Penicillin-Streptomycin Solution
- D-(+)-Glucose
- Sodium Azide
- Polyoxyethylene 20 oleyl ether (PEG)
- Tin (II) chloride.

Ethanol was obtained from Hayman Ltd.
Acetonitrile, Acetone, and methanol were obtained from Fisher Scientific.
Aquasafe 500 plus® liquid scintillation fluid was obtained from Zinsser Analytic.
Solvable® was supplied by PerkinElmer.
Rainin Pos-D® pipettes were supplied by Rainin Instrument.
Retsch mill mixer MM400 supplied by Retsch Ltd.

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Simple Antibacterial Handwash was supplied by Simple Health and Beauty Limited. Zimmer® electric dermatome (Ref 88 21 06) was supplied by Zimmer Orthopaedic Products.

All other materials were obtained by Charles River.

3.2 Confirmation of Radiochemical Purity of [^{14}C]-Cyproconazole

A single aliquot (10 µL) of the [^{14}C]-Cyproconazole stock solution was diluted in acetonitrile (200 µL). A U.V. standard was prepared, Cyproconazole (1 mg) was added to a vial and mobile phase (1 mL) added and mixed until in solution. An aliquot (25 µL) of [^{14}C]-Cyproconazole in acetonitrile was transferred to a vial along with U.V. standard (25 µL) and acetonitrile (50 µL).

A single aliquot (10 µL) of the [^{14}C]-Isopyrazam stock solution was diluted in acetonitrile (200 µL). A U.V. standard was prepared, Isopyrazam (1 mg) was added to a vial and acetonitrile (1 mL) added and mixed until in solution. An aliquot (50 µL) of [^{14}C]-Isopyrazam in acetonitrile was transferred to a vial along with U.V. standard (50 µL) and acetonitrile (50 µL).

The radiochemical purity of [^{14}C]-Cyproconazole and [^{14}C]-Isopyrazam in the solutions was determined by high performance liquid chromatography (HPLC) using the following equipment and conditions:

Equipment

Packard 150TR HPLC System
Scintillant: FlowlogicU (1:1, v/v)

Conditions

Column: Hichrom ACE C18 (250 mm x 4.0 mm, 5 µm)
Mobile Phase A: Milli Q Water
Mobile Phase B: Acetonitrile
Mobile Phase Conditions: Gradient

Time (min)	Mobile Phase A (%)	Mobile Phase 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

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Run Time: 35 min
Flow Rate: 1.0 mL/min
Column Temperature: 40°C
Auto-sampler Temperature: 4°C
U.V. Detector Wavelength: 220 nm

Data was captured by Atlas 2002 (Thermos LabSystems) R1

The chemical authenticity of [^{14}C]-Cyproconazole was confirmed by co-chromatography with authentic non-radiolabelled Cyproconazole. The radiochemical purity of [^{14}C]- Cyproconazole was determined to be 100%. A representative HPLC chromatogram is presented in Appendix 4.

The chemical authenticity of [^{14}C]-Isopyrazam was confirmed by co-chromatography with authentic non-radiolabelled Isopyrazam. The radiochemical purity of [^{14}C]- Isopyrazam was determined to be 99.6%. A representative HPLC chromatogram is presented in Appendix 5.

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

Three aliquots (10 µL) of [^{14}C]-Cyproconazole stock solution were removed into vials. Acetonitrile (10 mL) was added to each vial and the contents mixed. An aliquot (1 mL) was removed from each vial, mixed with scintillation fluid (10 mL) and analysed by liquid scintillation counting.

By radioactivity, the concentration of [^{14}C]-Cyproconazole in the stock solution was 6.78 mg/mL. The stock solution was homogeneous with a coefficient of variation (CV) of 1.05%.

3.4 Confirmation of Concentration of [^{14}C]-Isopyrazam Stock Solution

Three aliquots (10 µL) were removed from [^{14}C]-Isopyrazam stock solution into vials. Acetonitrile (10 mL) was added to each vial and the contents mixed. Duplicate 2 mL aliquots were removed from each vial, mixed with scintillation fluid (10 mL) and analysed by liquid scintillation counting.

By radioactivity, the concentration of [^{14}C]-Isopyrazam in the stock solution was 4.838 mg/mL. The stock solution was homogeneous with a coefficient of variation (CV) of 0.76%.

3.5 Human Skin Samples

Six samples of full-thickness human skin (4 abdomen, 1 abdomen/thigh and 1 abdomen/breast) were obtained from donors aged 32 to 62 years old. Four of the samples were obtained from NHS Lothian, St. John's Hospital, Livingston, UK. On arrival at Charles River, the samples were cleaned of subcutaneous fat and connective tissue using a scalpel

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blade. The skin samples were washed in cold running water and dried using tissue paper. The skin samples were then cut into smaller pieces (where appropriate), wrapped in aluminium foil, placed into self-sealing plastic bags and stored in a freezer set to maintain a temperature of -20°C until they were used in the study. Two of the samples were obtained from Tissue Solutions. On arrival at Charles River, the samples were placed into self-sealing plastic bags and stored in a freezer set to maintain a temperature of -20°C until they were 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 sample details are shown in Appendix 6.

3.6 Preparation of Split-Thickness Skin

Human 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 membranes were then laid out onto aluminium foil and the thickness of the membranes measured using a micrometer. The split-thickness membranes were stored in a freezer set to maintain a temperature of -20°C. The thickness of the full-thickness and split-thickness skin membranes is provided in Appendix 7.

3.7 Static Diffusion Cell Apparatus

A static diffusion cell system (PermeGear Inc) was used (see photograph below). 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 (31.4°C to 32.5°C).

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

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The surface area of exposed skin within the cells was 3.14 cm^2. The receptor chamber volume was nominally 10 mL, with each receptor chamber individually marked with the actual volume by the manufacturer.

3.8 Receptor Fluid

The following receptor fluids were chosen for use in a solubility test to determine which receptor fluid to use for test item permeability measurements in this study.

Receptor Fluid A: Tissue culture medium (MEME) containing polyoxyethylene 20 oleyl ether (PEG, 6%, w/v), glucose (1%, w/v), sodium azide (0.01%, w/v), streptomycin (0.1 mg/mL) and penicillin G (100 units/mL).

Receptor Fluid B: Phosphate buffered saline: ethanol (1:1, v/v).

These were degassed by sonication

3.9 Solubility of the Test Items in Receptor Fluid

Cyproconazole was predicted to have a water solubility of 93 mg/L at 22ºC (The Pesticide Manual, Fourteenth Edition). For an application of 10 µL/cm^2 over a 3.14 cm^2 application area, for the highest concentration formulation (80 g/L), 31.4 µL of test preparation has been applied to each skin sample. Theoretically, if 100% of Cyproconazole was absorbed, this would have resulted in a test item concentration in the receptor fluid of 251 mg/L.

Isopyrazam was predicted to have a water solubility of 1.05 mg/L at 25ºC (Syngenta, MSDS). For an application of 10 µL/cm^2 over a 3.14 cm^2 application area, for the highest concentration formulation (125 g/L), 31.4 µL of test preparation has been applied to each skin sample. Theoretically, if 100% of Isopyrazam was absorbed, this would have resulted in a test item concentration in the receptor fluid of 393 mg/L.

Subsequently, the solubility of the test item in Receptor Fluid A and Receptor Fluid B was determined to select a suitable receptor fluid

3.10 Solubility Assessment

3.10.1 Preparation of radiodiluted test items

Cyproconazole Technical (307 mg) and [^{14}C]-Cyproconazole stock solution (50 µL) were added to a 1 mL volumetric flask. Methanol was added to the calibration line and the contents mixed.

[^{14}C]-Isopyrazam stock solution (130 µL) was transferred into a volumetric flask (2 mL) and the solvent removed under nitrogen gas. Isopyrazam Technical (516 mg) was added to the volumetric flask and acetone added to the calibration line and the contents mixed.

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Three aliquots (10 µL) of the radiodilutions were taken into glass vials, mixed with methanol:scintillation fluid (1:10, v/v; 11 mL) and analysed by liquid scintillation counting

By radioactivity, the concentration of radiodiluted Cyproconazole was determined to be 302.31 mg/mL. The radiodiluted Cyproconazole was homogeneously distributed within the solution with a CV of 0.92% and the specific activity was determined to be 0.0675 µCi/mg.

By radioactivity, the concentration of radiodiluted Isopyrazam was determined to be 250.95 mg/mL. The radiodiluted Isopyrazam was homogeneously distributed within the solution with a CV of 0.31% and the specific activity was determined to be 0.0818 µCi/mg.

3.10.2 Solubility test

Radiodiluted Cyproconazole (*ca* 63 mg) was transferred into three 25 mL volumetric flasks. Radiodiluted Isopyrazam (*ca* 98 mg) was transferred into a further three 25 mL volumetric flasks. The solvent was dried off, under a gentle stream of nitrogen gas for receptor fluid samples. The flasks were then filled to the 25 mL line with either Receptor Fluid A, Receptor Fluid B, or methanol (positive control for Cyproconazole) or acetone (positive control for Isopyrazam). The solutions were mixed and heated for 1 h at *ca* 32°C and then centrifuged at 2000 *g* for 5 min at 20°C. Duplicate aliquots (1 mL) of the resultant supernatant were taken, mixed with scintillation fluid (10 mL) and analysed by liquid scintillation counting.

The results are provided in the following tables:

Sample Type	Concentration of Cyproconazole in Solution (g/L)	% of Target Cyproconazole Concentration (2.51 g/L)
Receptor Fluid A	0.5525	21.93
Receptor Fluid B	2.3794	94.42
Methanol	2.5640	101.75

Receptor Fluid B was chosen as receptor fluid since Cyproconazole dissolved in this receptor fluid at *ca* 9.5-fold greater than the total applied dose for the concentrate would do in the receptor chamber (10 mL). This was greater than Receptor Fluid A (*ca* 2.2-fold greater than the total applied dose for the concentrate). The solubility that was achieved for Cyproconazole was considered the highest achievable concentration in the most suitable receptor fluids that does not interfere with the test system.

Sample Type	Concentration of Isopyrazam in Solution (g/L)	% of Target Isopyrazam Concentration (3.93g/L)
Receptor Fluid A	1.0228	26.03
Receptor Fluid B	1.9828	50.45
Acetone	4.1369	105.27

Receptor Fluid B was chosen as receptor fluid since Isopyrazam dissolved in this receptor fluid at *ca* 5-fold greater than the total applied dose for the concentrate would do in the

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receptor chamber (10 mL). This was greater than Receptor Fluid A (*ca* 2.6-fold greater than the total applied dose for the concentrate). The solubility that was achieved for Isopyrazam was considered the highest achievable concentration in the most suitable receptor fluids that do not interfere with the test system.

3.11 Formulation of Test Preparations for Stability and Volatility Assessments

3.11.1 [^{14}C]-Cyproconazole in test preparations

Summary of the mass of each item for [^{14}C]-Cyproconazole formulation concentrate, Spray Dilution 1 and Spray Dilution 2 is provided in the following table.

Test Preparation	[^{14}C]-Cyproconazole Formulation Concentrate	[^{14}C]-Cyproconazole Spray Dilution 1	[^{14}C]-Cyproconazole Spray Dilution 2
Volume of [^{14}C]-Cyproconazole stock solution	220 µL	253 µL	N/A
Mass of Cyproconazole	0.20206 g	N/A	N/A
Volume of radiodiluted Cyproconazole added to test preparation	1.6 mL	N/A	N/A
Mass of Isopyrazam	0.24925 g	0.00269 g	N/A
Mass of blank formulation	1.71672 g	0.01799 g	N/A
Volume of Spray Dilution 1	N/A	N/A	586 µL
Volume of CIPAC D water	N/A	1.98 mL	1414 µL
Concentration of Cyproconazole by radioactivity	68.87 g/L	0.64 g/L	0.18 g/L
Target concentration of Cyproconazole	80 g/L	0.8 g/L	0.2 g/L
Percentage of target	86.09%	79.95%	92.02%
CV	0.42%.	0.34%	0.35%

N/A = not applicable

3.11.2 Preparation of radiodiluted [^{14}C]-Cyproconazole for test preparation 1

Cyproconazole Technical (202.06 mg) was added to a volumetric flask (2 mL). [^{14}C]-Cyproconazole stock solution (0.220 mL) was transferred into the volumetric flask. Acetone was added to the volumetric flask up to the 2 mL line and the contents were mixed until a clear solution was formed. Three aliquots (10 µL) were removed, mixed with methanol:scintillation fluid (1:10, v/v, 11 mL) and analysed by liquid scintillation counting.

By radioactivity, the concentration of the radiodiluted Cyproconazole was determined to be. 100.06 mg/mL. The radiodiluted Cyproconazole was homogeneously distributed in the solution, with a CV of 1.99%. The specific activity of the radiodiluted test item was calculated to be 0.431 µCi/mg.

3.11.3 Preparation of [^{14}C]-Cyproconazole in the formulation concentrate (Test Preparation 1)

The radiodiluted Cyproconazole (1.6 mL, prepared in Section 3.11.2) was transferred into a glass vial and the solvent dried off under a gentle stream of nitrogen gas. Non-radiolabelled Isopyrazam Technical (249.25 mg) was added to the radiodiluted Cyproconazole. Glass

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beads and blank formulation of A19022A (1716.72 mg) were added to the vial and the contents mixed using a mill mixer for 10 min at 25 oscillations/s. A magnetic stirrer bar was added to the vial and placed onto a magnetic stirrer plate. Six aliquots (31.4 µL) were removed, mixed with methanol:scintillation fluid (1:10, v/v, 11 mL) and analysed by liquid scintillation counting.

Further mixing was required, therefore, the vial containing Test Preparation 1 was vortex mixed for 2 min and a further six aliquots (15.7 µL) were removed, mixed with methanol:scintillation fluid (1:10, v/v, 11 mL) and analysed by liquid scintillation counting.

By radioactivity, the concentration of the Cyproconazole in the Formulation Concentrate was determined to be 68.87 g/L. This was 86.09% of the target concentration (80 g/L). The radiodiluted Cyproconazole was homogeneously distributed within the test preparation with a CV of 0.42%. The Formulation Concentrate was accepted for dosing for the stability and volatility assessments.

3.11.4 Preparation of [^{14}C]-Cyproconazole in spray dilution 1 (Test Preparation 2)

Radiolabelled Cyproconazole stock solution (0.253 mL) was transferred to a glass vial containing glass beads and the solvent dried off under a gentle stream of nitrogen gas. Isopyrazam Technical (2.69 mg) was added to the vial. Blank formulation of A19022A (17.99 mg) was added and the contents mixed using a mill mixer for 10 minutes at 25 oscillations/s. CIPAC D water (1.98 mL) was added in small aliquots to the vial and the contents were mixed between each aliquot using a vortex mixer. The vial was further mill mixed for 10 min, vortex mixed for 1 min and placed onto a magnetic stirring plate to mix. Six aliquots (15.7 µL), were removed, mixed with methanol:scintillation fluid (1:10, v/v, 11 mL) and analysed by liquid scintillation counting.

By radioactivity, the concentration of the Cyproconazole in spray dilution 1 was determined to be 0.64 g/L. This was 79.95% of the target concentration (0.8 g/L). The radiodiluted Cyproconazole was homogeneously distributed within the test preparation with a CV of 0.34%. Therefore, Spray Dilution 1 was accepted for dosing for the stability and volatility assessments.

3.11.5 Preparation of [^{14}C]-Cyproconazole in spray dilution (Test Preparation 3)

An aliquot (586 µL) of spray dilution 1 was transferred into a vial (see Section 3.11.4) CIPAC Standard Water D (1.414 mL) was added to the vial along with a magnetic stirrer bar. The contents of the vial were mixed on a magnetic stirrer plate. Six aliquots (31.4 µL), were removed, mixed with methanol:scintillation fluid (1:10, v/v, 11 mL) and analysed by liquid scintillation counting.

By radioactivity, the concentration of the Cyproconazole in spray dilution 2 was determined to be 0.18 g/L. This was 92.02% of the target concentration (0.2 g/L). The radiodiluted Cyproconazole was homogeneously distributed within the test preparation with a CV of

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0.35%. Therefore, Spray Dilution 2 was accepted for dosing for the stability and volatility assessments.

3.11.6 [^{14}C]-Isopyrazam formulation concentrate, spray dilution 1 and spray dilution 2 (Test Preparations 4, 5 and 6)

[^{14}C]-Isopyrazam Formulation Concentrate, Spray Dilution 1 and Spray Dilution 2 were prepared in a similar manner to [^{14}C]-Cyproconazole test preparations detailed in Sections 3.11.2-3.11.5, utilising [^{14}C]-Isopyrazam and non radiolabelled Cyproconazole. Summary of each item is provided in the following table.

Test Preparation	[^{14}C]-Isopyrazam Formulation Concentrate	[^{14}C]-Isopyrazam Spray Dilution 1	[^{14}C]-Isopyrazam Spray Dilution 2
Volume of [^{14}C]-Isopyrazam stock solution	250 µL	775 µL	N/A
Mass of Isopyrazam	0.33494 g	N/A	N/A
Volume of radiodiluted Isopyrazam added to test preparation	1.53 mL	N/A	N/A
Mass of Cyproconazole	0.16158 g	0.00266 g	N/A
Mass of blank formulation	1.71470 g	0.02676 g	N/A
Volume of Spray Dilution 1	N/A	N/A	500 µL
Volume of CIPAC D water	N/A	2.97 mL	1500 µL
Concentration of Isopyrazam by radioactivity	122.26 g/L	1.33 g/L	0.34 g/L
Target concentration of Isopyrazam	125 g/L	1.25 g/L	0.31 g/L
Percentage of target	97.81%	106.49%	110.09%
CV	5.29%.	0.31%	1.01%

3.12 Stability and Volatility Assessments

3.12.1 Volatility Assessment

Sections of aluminium foil were mounted onto a static cell containing phosphate buffered saline. The static cell was placed in the manifold and connected to the circulating waterbath (heated to maintain a surface temperature of 32°C). [^{14}C]-Cyproconazole in the Formulation Concentrate was applied to the exposed area of 6 samples of aluminium foil using a positive displacement pipette set to deliver 31.4 µL (10 µL/cm^2). Five representative aliquots were collected into scintillation vials at the time of dosing. The aliquots were dissolved in methanol:scintillation fluid (1:10, v/v; 11 mL) and analysed by liquid scintillation counting.

[^{14}C]-Cyproconazole in Spray Dilution 1 and Spray Dilution 2 and [^{14}C]-Isopyrazam in the Formulation Concentrate, Spray Dilution 1 and Spray Dilution 2 were also applied to 6 samples of aluminium foil each as described for Test Preparation 1. The results of the representative aliquots are provided in the table overleaf.

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Test Item	Target Test Item Concentration (g/L)	Test Item Concentration (g/L)	
		Mean	CV (%)
[^{14}C]-Cyproconazole Formulation Concentrate	80	83.48	1.30
[^{14}C]-Cyproconazole Spray Dilution 1	0.8	0.62	0.75
[^{14}C]-Cyproconazole Spray Dilution 2	0.2	0.18	0.55
[^{14}C]-Isopyrazam Formulation Concentrate	125	125.73	1.70
[^{14}C]-Isopyrazam Spray Dilution 1	1.25	1.31	0.61
[^{14}C]-Isopyrazam Spray Dilution 2	0.31	0.34	0.40

Immediately after dosing, three cells for each test preparation were transferred into a pre-weighed pot containing methanol:water (1:1, v/v). The samples were left to extract overnight, then removed from the pots and duplicate aliquots (1 mL) taken, weighed, and analysed by liquid scintillation counting. At 24 h post dose the process described above was repeated. The results of this analysis are provided in the following tables.

Test Preparation	[^{14}C]-Cyproconazole Formulation Concentrate		[^{14}C]-Cyproconazole Spray Dilution 1		[^{14}C]-Cyproconazole Spray Dilution 2	
Distribution	% Applied Dose		% Applied Dose		% Applied Dose	
Termination Timepoint (h)	0	24	0	24	0	24
Mean Mass Balance (n = 3)	99.58	99.73	96.15	101.24	99.96	88.42

The mean mass balance for the Cyproconazole Spray Dilution 2 (0.2 g/L) was slightly outside the OECD guideline criteria (100%±10%) during the volatility assessment. However, this was due to one low replicate. All other mean data were within the acceptable range.

Test Preparation	[^{14}C]-Isopyrazam Formulation Concentrate		[^{14}C]-Isopyrazam Spray Dilution 1		[^{14}C]-Isopyrazam Spray Dilution 2	
Distribution	% Applied Dose		% Applied Dose		% Applied Dose	
Termination Timepoint (h)	0	24	0	24	0	24
Mean Mass Balance (n = 3)	102.03	109.76	90.11	98.81	96.30	101.35

The test items were not deemed to be volatile under the experimental conditions.

The individual volatility data for all the test preparations are provided in Appendix 9.

3.12.2 Stability Assessment

Prior to dosing, three weighed aliquots from [^{14}C]-Cyproconazole Formulation Concentrate (31.4 µL), Spray Dilution 1 (31.4 µL) and Spray Dilution 2 (100 µL) were removed from each test preparation. Acetonitrile:Water (1:1, v/v) was added to each aliquot, 20 mL for the Formulation Concentrate samples, 0.1686 mL for Spray Dilution 1 samples and 0.1 mL for Spray Dilution 2 samples. One further sample (31.4 µL) was taken from [^{14}C]-Cyproconazole Formulation Concentrate, mixed with 130 µL of acetonitrile prior to dosing to confirm the radiochemical purity in the sample.

Prior to dosing, three weighed aliquots from [^{14}C]-Isopyrazam Formulation Concentrate (15.7 µL), Spray Dilution 1 (31.4 µL) and Spray Dilution 2 (100 µL) were removed from each test preparation. Acetonitrile:water (1:1, v/v) was added to each aliquot, 20 mL for the

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Formulation Concentrate samples, 0.3486 mL for Spray Dilution 1 samples and 0.2 mL for Spray Dilution 2 samples. One further sample (62.8 µL) was taken from [^{14}C]-Isopyrazam Formulation Concentrate, mixed with 240 µL of acetonitrile prior to dosing to confirm the radiochemical purity in the sample.

At 24 h post dose the process described above was repeated. All samples were analysed by HPLC using the equipment and conditions stated in Section 3.2. The results of this analysis are provided in the following table.

Sample Description	Mean Test Item Concentration (mg/mL)[a]	Percentage of Target	Radiochemical Purity Result (%)
Pre-dose [^{14}C]-Cyproconazole Formulation Concentrate	88.27	110.33	100
24 h Post-dose [^{14}C]-Cyproconazole Formulation Concentrate	108.54[b]	135.67	100
Pre-dose [^{14}C]-Cyproconazole Spray Dilution 1	0.65	80.74	100
24 h Post-dose[^{14}C]-Cyproconazole Spray Dilution 1	0.63	79.01	100
Pre-dose [^{14}C]-Cyproconazole Spray Dilution 2	0.20	99.74	100
24 h Post-dose [^{14}C]-Cyproconazole Spray Dilution 2	0.19	93.02	100
Pre-dose [^{14}C]-Isopyrazam Formulation Concentrate	125.43	100.35	99.5
24 h Post-dose [^{14}C]-Isopyrazam Formulation Concentrate	147.03[b]	117.62	99.7
Pre-dose [^{14}C]-Isopyrazam Spray Dilution 1	1.41	112.62	99.6
24 h Post-dose [^{14}C]-Isopyrazam Spray Dilution 1	1.41	112.99	99.6
Pre-dose [^{14}C]-Isopyrazam Spray Dilution 2	0.36	116.92	99.5
24 h Post-dose [^{14}C]-Isopyrazam Spray Dilution 2	0.32	101.77	99.3

[a] n = 3 with the exception of [b] where n = 2

Based upon the variation observed in the results above, it was decided to prepare all test preparations on the day of dosing for application of each test preparation to skin samples.

3.13 Static Diffusion Cell Preparation

Split-thickness skin was removed from a freezer set to maintain a temperature of -20°C and allowed to reach ambient temperature. The receptor chambers were placed in a manifold and they were connected to a circulating waterbath. Magnetic stirrer bars were placed in the receptor fluid chambers which were filled with the receptor fluid. Sections of split-thickness skin, *ca* 3 x 3 cm, were cut and mounted in the diffusion cells between the donor and receptor chamber. The donor chamber was tightened into place with a clamp. The receptor fluid volume was made up to the pre calibrated line on the collection arm. No air bubbles were present in the receptor fluid chamber.

3.14 Barrier Integrity Assessment

Each cell was filled above the calibration line on the receptor fluid arm and checked visually after to confirm that no cells were leaking (leak test). Any cell that was found to be leaking was replaced and the leak test was performed again. Phosphate buffered saline (3 mL) was added to the donor chamber. This was allowed to equilibrate for 30 min. The electrical resistance was then measured using a Tinsley Databridge (Model 6401) set at low voltage

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alternating current, 1000 Hz with a maximum voltage of 300 mV root-mean-squared (rms) in the parallel equivalent circuit mode. Any skin sample exhibiting a resistance less than 4 kΩ was excluded from subsequent absorption measurements. A cross reference of skin cell number, donor number and electrical resistance (kΩ) is presented in Appendix 8. The phosphate buffered saline was removed from the skin surface and the skin was rinsed with water (2-3 mL) and dried with tissue paper.

3.15 Predose Receptor Fluid Collection

Prior to dosing, a 300 µL (6 x 50 µL aliquots) sample of receptor fluid was removed from the receptor chamber collection arm. 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. The receptor fluid samples were mixed with methanol:scintillation fluid (1:10, (v/v), 11 mL) and analysed by liquid scintillation counting. Following sample collection, the receptor chamber collection arm was sealed with Parafilm® to prevent evaporation of receptor fluid from the receptor chamber.

3.16 Formulation of Test Preparations

3.16.1 [^{14}C]-Cyproconazole in test preparations

Test Preparations 1-6 were prepared in a similar manner to process described in Section 3.11. A summary of the mass of each item for [^{14}C]-Cyproconazole formulation concentrate, Spray Dilution 1 and Spray Dilution 2 is provided in the following table.

Test Preparation	[^{14}C]-Cyproconazole Formulation Concentrate	[^{14}C]-Cyproconazole Spray Dilution 1	[^{14}C]-Cyproconazole Spray Dilution 2
Volume of [^{14}C]-Cyproconazole stock solution	330 µL	371 µL	N/A
Mass of Cyproconazole	0.31373 g	N/A	N/A
Volume of radiodiluted Cyproconazole added to test preparation	1.57 mL	N/A	N/A
Mass of Isopyrazam	0.38624 g	0.00397 g	N/A
Mass of blank formulation	2.60985 g	0.02548 g	N/A
Volume of Spray Dilution 1	N/A	N/A	500 µL
Volume of CIPAC D water	N/A	2.97 mL	1.5 mL
Concentration of Cyproconazole by radioactivity	83.75 g/L	0.86 g/L	0.22 g/L
Target concentration of Cyproconazole	80 g/L	0.8 g/L	0.2 g/L
Percentage of target	104.69%	107.19%	107.57%
CV	0.43%	0.55%	0.30%

3.16.2 [^{14}C]-Isopyrazam in test preparations

A summary of the mass of each item for [^{14}C]-Isopyrazam formulation concentrate, Spray Dilution 1 and Spray Dilution 2 is provided in the table overleaf.

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Test Preparation	[^{14}C]-Isopyrazam Formulation Concentrate	[^{14}C]-Isopyrazam Spray Dilution 1	[^{14}C]-Isopyrazam Spray Dilution 2
Volume of [^{14}C]-Isopyrazam stock solution	375 µL	775 µL	N/A
Mass of Isopyrazam	0.46168 g	N/A	N/A
Volume of radiodiluted Isopyrazam added to test preparation	1.67 mL	N/A	N/A
Mass of Cyproconazole	0.24446 g	0.00235 g	N/A
Mass of blank formulation	2.59780 g	0.02613 g	N/A
Volume of Spray Dilution 1	N/A	N/A	500 µL
Volume of CIPAC D water	N/A	2.97 mL	1.629 mL
Concentration of Isopyrazam by radioactivity	123.81 g/L	1.36 g/L	0.32 g/L
Target concentration of Isopyrazam	125 g/L	1.25 g/L	0.31 g/L
Percentage of target	99.05%	108.54%	104.69%
CV	1.47%.	0.22%	0.52%

By radioactivity, the concentration of the [^{14}C]-Cyproconazole in the Formulation Concentrate was determined to be 83.75 g/L. This was 104.69% of the target concentration (80 g/L). The [^{14}C]- Cyproconazole was homogeneously distributed within the test preparation with a CV of 0.43%. Therefore, the Formulation Concentrate was accepted for dosing.

By radioactivity, the concentration of the [^{14}C]-Cyproconazole in Spray Dilution 1 was determined to be 0.86 g/L. This was 107.19% of the target concentration (0.8 g/L). [^{14}C]-Cyproconazole was homogeneously distributed within the test preparation with a CV of 0.55%. Therefore, Spray Dilution 1 was accepted for dosing.

By radioactivity, the concentration of the [^{14}C]-Cyproconazole in Spray Dilution 2 was determined to be 0.22 g/L. This was 107.57% of the target concentration (0.2 g/L). The [^{14}C]-Cyproconazole was homogeneously distributed within the test preparation with a CV of 0.30%. Therefore, Spray Dilution 2 was accepted for dosing.

By radioactivity, the concentration of the [^{14}C]-Isopyrazam in the Formulation Concentrate was determined to be 123.81 g/L. This was 99.05% of the target concentration (125 g/L). The [^{14}C]-Isopyrazam was homogeneously distributed within the test preparation with a CV of 1.47%. Therefore, the Formulation Concentrate was accepted for dosing.

By radioactivity, the concentration of the [^{14}C]-Isopyrazam in Spray Dilution 1 was determined to be 1.40 g/L. This was 111.78% of the target concentration (1.25 g/L). [^{14}C]-Isopyrazam was homogeneously distributed within the test preparation with a CV of 0.37%. Therefore Spray Dilution 1 was further diluted. The test preparation (1.5 mL) was transferred into a new vial, CIPAC D water (75 µL) added and mixed on a magnetic stirring plate. A further six aliquots (31.4 µL) were removed, mixed with methanol:scintillation fluid (1:10, v/v, 11 mL) and analysed by liquid scintillation counting. By radioactivity, the concentration of the [^{14}C]-Isopyrazam in Spray Dilution 1 was determined to be 1.36 g/L. This was 108.54% of the target concentration (1.25 g/L). [^{14}C]-Isopyrazam was homogeneously distributed within the test preparation with a CV of 0.22%. Therefore, Spray Dilution 1 was accepted for dosing.

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By radioactivity, the concentration of the [^{14}C]-Isopyrazam in Spray Dilutions 2 was determined to be 0.32 g/L. This was 104.69% of the target concentration (0.31 g/L). The [^{14}C]-Isopyrazam was homogeneously distributed within the test preparation with a CV of 0.52%. Therefore, Spray Dilutions 2 was accepted for dosing.

3.17 Application of Test Preparations to Human Skin

[^{14}C]-Cyproconazole Formulation Concentrate (Test Preparation 1) was applied over the stratum corneum surface of the exposed skin of 8 split-thickness samples using an MR50 Rainin positive displacement pipette set to deliver 31.4 µL (10 µL/cm^2). Seven representative aliquots of each test preparation were collected into scintillation vials at the time of dosing. The aliquots were dissolved in methanol:scintillation fluid (1:10, v/v; 11 mL) and analysed by liquid scintillation counting.

[^{14}C]-Cyproconazole Spray Dilutions 1 and 2 (Test Preparation 2 and 3) and [^{14}C]-Isopyrazam in Formulation Concentrate, Spray Dilutions 1 and 2 (Test Preparations 4, 5 and 6) were also applied to 8 samples of split-thickness skin each as described for Test Preparation 1. The results of the representative aliquots are provided in the following table.

Test Item	Target Test Item Concentration (g/L)	Test Item Concentration (g/L)	
		Mean	CV (%)
[^{14}C]-Cyproconazole Formulation Concentrate	80	83.65	1.17
[^{14}C]-Cyproconazole Spray Dilution 1	0.8	0.84	0.74
[^{14}C]-Cyproconazole Spray Dilution 2	0.2	0.21	0.49
[^{14}C]-Isopyrazam Formulation Concentrate	125	123.26	1.12
[^{14}C]-Isopyrazam Spray Dilution 1	1.25	1.33	0.86
[^{14}C]-Isopyrazam Spray Dilution 2	0.31	0.33	0.27

3.18 Test Item Concentration and Stability Confirmation

Prior to dosing, 3 aliquots of each [^{14}C]-Cyproconazole and [^{14}C]-Isopyrazam test preparations were taken to confirm the test item concentration by HPLC. Water:acetonitrile (1:1, v/v) was added to all aliquots. A summary of the sampling aliquots are provided in the following table:

Test Preparation	Number of Aliquots	Aliquot Sample (µL)	Water:acetonitrile added (mL)
[^{14}C]-Cyproconazole Formulation Concentrate	3	25	20
[^{14}C]-Cyproconazole Spray Dilution 1	3	31.4	0.219
[^{14}C]-Cyproconazole Spray Dilution 2	3	100	0.1
[^{14}C]-Isopyrazam Formulation Concentrate	3	15.7	20
[^{14}C]-Isopyrazam Spray Dilution 1	3	31.4	0.349
[^{14}C]-Isopyrazam Spray Dilution 2	3	100	0.2

A further sample was taken from [^{14}C]-Cyproconaole Formulation Concentrate and [^{14}C]-Isopyrazam Formulation Concentrate prior to dosing to confirm the radiochemical purity in each sample.

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Immediately after dosing the process described above was repeated. All samples were analysed using the equipment and conditions stated in Section 3.2.

The radiochemical purity results and test preparation concentrations by HPLC are provided in the following table.

Sample Description	Mean Test Item Concentration (mg/mL)	Percentage of Target	Radiochemical Purity Result (%)
Pre-dose [^{14}C]-Cyproconazole Formulation Concentrate	88.04	110.05	100
Post-dose [^{14}C]-Cyproconazole Formulation Concentrate	85.81	107.26	100
Pre-dose [^{14}C]-Cyproconazole Spray Dilution 1	0.90	112.58	100
Post-dose [^{14}C]-Cyproconazole Spray Dilution 1	0.93	116.26	100
Pre-dose [^{14}C]-Cyproconazole Spray Dilution 2	0.24	118.72	100
Post-dose [^{14}C]-Cyproconazole Spray Dilution 2	0.23	117.18	100
Pre-dose [^{14}C]-Isopyrazam Formulation Concentrate	120.66	96.53	99.5
Post-dose [^{14}C]-Isopyrazam Formulation Concentrate	118.76	95.00	99.4
Pre-dose [^{14}C]-Isopyrazam Spray Dilution 1	1.34	107.20	99.7
Post-dose [^{14}C]-Isopyrazam Spray Dilution 1	1.36	108.80	99.3
Pre-dose [^{14}C]-Isopyrazam Spray Dilution 2	0.37	117.91	99.6
Post-dose [^{14}C]-Isopyrazam Spray Dilution 2	0.35	112.86	99.5

The radiochemical purity results confirmed that the test items were stable over the dosing period.

The concentration of Cyproconazole in the Concentrate Formulation, Spray Dilutions 1 and 2 (Test Preparations 1, 2 and 3) were within 15% of those determined by radioactivity; this remained between 107-119% of the target concentration throughout dosing.

The concentration of Isopyrazam in the Concentrate Formulation and Spray Dilutions 1 and 2 (Test Preparations 4, 5 and 6) were within15% of those determined by radioactivity; this remained between 95-118% of the target concentration throughout dosing.

3.19 Receptor Fluid Sampling

Receptor fluid aliquots were collected at 2, 4, 6, 8, 12 and 24 h post dose as described in Section 3.15. All the receptor fluid samples were mixed with methanol:scintillation fluid (1:10, v/v; 11 mL) and analysed by liquid scintillation counting.

3.20 Terminal Exposure (6 h Post Dose)

After dosing the exposure was terminated (6 h) by application of a commercial hand wash soap (*ca* 50µL) to the skin. With the soap on, the skin was gently rubbed with a tissue swab. The skin was then rinsed with *ca* 5 mL of a *ca* 2% (v/v) commercial soap solution (Simple Antibacterial Hand wash/Elga water). The soap solution was applied in 1 mL aliquots, and each aliquot was aspirated three times with a pipette. The skin was dried with a tissue swab.

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The process was repeated and the skin was dried with an additional tissue swab. The soap solution (skin wash) was pooled into a single pre-weighed vial. Acetonitrile (10 mL) was added to each skin wash sample that had [^{14}C]-Cyproconazole Formulation Concentrate applied. Duplicate aliquots (1 mL) were removed from each skin wash sample, mixed with scintillation fluid (10 mL) and analysed by liquid scintillation counting. The tissue swabs and pipette tips were analysed by liquid scintillation counting.

3.21 Terminal Exposure (24 h Post Dose)

After an 18-hour monitoring period, 24 hours post dose skin was washed again and samples analysed as described in Section 3.20. The sealing clamp and the donor chamber were removed. The donor chamber was transferred to a pre-weighed pot containing methanol.

Skin was removed from the cell and placed on a piece of tissue (24 h tissue swab) to remove any remaining receptor fluid from the underside of the skin. The tissue swabs were placed into a scintillation vial, mixed with methanol:scintillation fluid (1:10, v/v; 11 mL) and then analysed by liquid scintillation counting.

The stratum corneum was removed with 20 successive tape strips. Each tape strip was placed into an individual vial containing methanol:scintillation fluid (1:10, v/v; 11 mL) and then analysed by liquid scintillation counting. Epidermis was not removed during the process. The skin under the cell flange (unexposed skin) and outside the donor chamber was cut away from the exposed skin. The exposed and unexposed skin samples were placed into separate vials containing Solvable® (3 mL). The skin samples were placed into a waterbath heated to *ca* 60°C to aid solubilisation. When fully dissolved, aliquots (1 mL) of each skin sample were mixed with stannous chloride solution (0.2 mg/mL in ethanol, 150 µL) and scintillation fluid (10 mL) and analysed by liquid scintillation counting.

The donor chambers were sonicated for *ca* 10 min then removed from the pots and duplicate aliquots (1 mL) taken, weighed, mixed with scintillation fluid (10 mL) and analysed by liquid scintillation counting.

The remaining receptor fluid in the receptor chamber was removed into individual vials and stored in a freezer set to maintain -20°C.

The receptor chamber was rinsed with 4 aliquots (10 mL) of methanol. The solvent was pooled as a single sample into a receptor wash pot. Duplicate aliquots (1 mL) taken from each receptor wash and donor wash pot, weighed, mixed with scintillation fluid (10 mL) and analysed by liquid scintillation counting.

3.22 Storage of Samples

After analysis all bulk samples were stored in a freezer set to maintain a temperature of -20°C.

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3.23 Quantification of Total Radioactivity

All samples were counted for 5 min together with representative blanks using a liquid scintillation analyser (Packard 2100-TR) with automatic quench correction by external standard. 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.

3.24 Electronic Data Acquisitions and Systems

Total radioactivity and sample weight data was acquired using DEBRA® (version 5.7.10.129) Management System (LabLogic Systems Limited, Paradigm House, 3 Melbourne Avenue, Broomhill, Sheffield, S10 2QJ, UK).

The data was transferred into Microsoft® Office Excel® 2007 (SP2 MSO) for calculation of result tables and graphs.

Chromatography data was acquired using Atlas (Thermo Electron Corporation, St George's Court, Hanover Business Park, Altrincham, Cheshire, WA14 5TP, United Kingdom).

3.25 Calculations

The following calculations were performed:

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

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

3.26 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.

3.27 Definitions

The definitions are taken directly from the OECD Guidance Document No. 28 and are provided in Appendix 10.

3.28 Protocol Deviation

The study was performed in accordance with the protocol for Charles River Study No.792932 with the following deviations.

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Protocol Section 12.4 and 12.6: The radiochemical purity of [^{14}C]-Cyproconazole and [^{14}C]-Isopyrazam in test preparations was confirmed in more than one sample. However as a conservative approach, the lowest radiochemical purity result was reported where more than one sample was analysed. There was no significant difference and any differences observed are likely due to analytical variation. Therefore, this was considered not to be an impact on the integrity of the study.

Protocol Section 14: Some aliquots used in the receptor fluid solubility assessment of Isopyrazam were analysed by liquid scintillation counting for 1 min instead of 5 min. Due to the relatively high levels of radioactivity in these samples, the d.p.m values were stable after 1 min. Therefore, the d.p.m values were deemed suitable for the calculation of the required solubility values and were considered not to have any impact on the integrity of the study.

4.0 RESULTS AND DISCUSSION

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

A summary of the results is provided in Tables 1 and 2.

4.1.1 [^{14}C]-Cyproconazole formulation concentrate (Test Preparation 1, 80 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]-Cyproconazole Formulation Concentrate (80 g/L). Overall, the absorption profiles looked similar for all samples. In all cells, there was an increase in absorption over the 24 h post dose period. The individual absorption profiles are provided in Figure 1. 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 Cyproconazole from [^{14}C]-Cyproconazole Formulation Concentrate 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 1.81 µg equiv./cm^2 (0.22% of the applied dose).

Following the skin wash at 6 h, 99.98% of the applied dose of Cyproconazole was washed off, with 0.58% removed with a skin wash at 24 h post dose. A proportion of the dose applied was recovered from the donor chamber (0.03%), 0.04% was found in the exposed skin and 0.01% was recovered from the receptor chamber wash. The mean total recovery was 100.88% of the applied dose.

The distribution of radioactivity (% applied dose) is provided in Table 3. The absorption profile is provided in Table 4 and Figure 2. The distribution by mass, of [^{14}C]-Cyproconazole at 24 h post dose is shown in Table 5. The absorption profile, by mass,

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is provided in Table 6 and Figure 3. The distribution of radioactivity in the stratum corneum, by mass, is provided in Table 7 and Figure 4.

4.1.2 [^{14}C]-Cyproconazole spray dilution 1 (Test Preparation 2, 0.8 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]-Cyproconazole Spray Dilution 1 (0.8 g/L). The absorption profiles looked similar for all samples. The individual absorption profiles are provided in Figure 5. 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 Cyproconazole from Spray Dilution 1 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 1.00 µg equiv./cm^2 (11.88% of the applied dose).

Following the skin wash at 6 h, 85.63% of the applied dose of Cyproconazole was washed off, with 2.48% removed with a skin wash at 24 h post dose. A proportion of the dose applied was recovered from the donor chamber (0.05%), 0.50% was found in the exposed skin and 0.23% was recovered from the receptor chamber wash. The mean total recovery was 101.05% of the applied dose.

The distribution of radioactivity (% applied dose) is provided in Table 8. The absorption profile is provided in Table 9 and Figure 6. The distribution by mass, of [^{14}C]-Cyproconazole at 24 h post dose is shown in Table 10. The absorption profile, by mass, is provided in Table 11 and Figure 7. The distribution of radioactivity in the stratum corneum, by mass, is provided in Table 12 and Figure 8.

4.1.3 [^{14}C]-Cyproconazole spray dilution 2 (Test Preparation 3, 0.2 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]-Cyproconazole Spray Dilution 2 (0.2 g/L). The absorption profiles looked similar for all samples. The individual absorption profiles are provided in Figure 9. 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 Cyproconazole from Spray Dilution 2 through human split-thickness skin was 0.02 µg equiv./cm^2/h during the 24 h experimental period. The amount penetrated at 24 h, as measured in the receptor fluid, was 0.47 µg equiv./cm^2 (22.05% of the applied dose).

Following the skin wash at 6 h, 73.97% of the applied dose of Cyproconazole was washed off, with 2.37% removed with a skin wash at 24 h post dose. A proportion of the dose applied was recovered from the donor chamber (0.04%), 0.50% was found in the exposed

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skin and 0.62% was recovered from the receptor chamber wash. The mean total recovery was 99.95% of the applied dose.

The distribution of radioactivity is provided in Table 13. The absorption profile is provided in Table 14 and Figure 10. The distribution by mass, of [^{14}C]-Cyproconazole at 24 h post dose is shown in Table 15. The absorption profile, by mass, is provided in Table 16 and Figure 11. The distribution of radioactivity in the stratum corneum, by mass, is provided in Table 17 and Figure 12.

4.1.4 [^{14}C]-Isopyrazam formulation concentrate (Test Preparation 4, 125 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]-Isopyrazam Formulation Concentrate (125 g/L). The absorption profiles looked similar for all samples. The individual absorption profiles are provided in Figure 13. 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 Isopyrazam from Formulation Concentrate through human split-thickness skin was 0.01 µg equiv./cm^2/h during the 24 h experimental period. The amount penetrated at 24 h, as measured in the receptor fluid, was 0.33 µg equiv./cm^2 (0.03% of the applied dose).

Following the skin wash at 6 h, 96.11% of the applied dose of Isopyrazam was washed off, with 0.20% removed with a skin wash at 24 h post dose. A proportion of the dose applied was recovered from the donor chamber (0.01%), 0.04% was found in the exposed skin and <0.01% was recovered from the receptor chamber wash. The mean total recovery was 96.45% of the applied dose.

The distribution of radioactivity (% applied dose) is provided in Table 18. The absorption profile is provided in Table 19 and Figure 14. The distribution by mass, of [^{14}C]-Isopyrazam at 24 h post dose is shown in Table 20. The absorption profile, by mass, is provided in Table 21 and Figure 15. The distribution of radioactivity in the stratum corneum, by mass, is provided in Table 22 and Figure 16.

4.1.5 [^{14}C]-Isopyrazam in spray dilution 1 (Test Preparation 5, 1.25 g/L) in human split-thickness skin membranes

A total of 8 samples of human split-thickness skin obtained from 4 different donors were dosed topically with [^{14}C]-Isopyrazam Spray Dilution 1 (1.25 g/L). The absorption profiles looked similar for all samples. The individual absorption profiles are provided in Figure 17. 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 Isopyrazam from Spray Dilution 1 through human split-thickness skin was 0.01 µg equiv./cm^2/h during the 24 h experimental period. The

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amount penetrated at 24 h, as measured in the receptor fluid, was 0.23 µg equiv./cm^2 (1.72% of the applied dose).

Following the skin wash at 6 h, 85.58% of the applied dose of Isopyrazam was washed off, with 7.26% removed with a skin wash at 24 h post dose. A proportion of the dose applied was recovered from the donor chamber (0.10%), 1.94% was found in the exposed skin and 0.04% was recovered from the receptor chamber wash. The mean total recovery was 98.71% of the applied dose.

The distribution of radioactivity (% applied dose) is provided in Table 23. The absorption profile is provided in Table 24 and Figure 18. The distribution by mass, of [^{14}C]-Isopyrazam at 24 h post dose is shown in Table 25. The absorption profile, by mass, is provided in Table 26 and Figure 19. The distribution of radioactivity in the stratum corneum, by mass, is provided in Table 27 and Figure 20.

4.1.6 [^{14}C]-Isopyrazam in spray dilution 2 (Test Preparation 6, 0.31 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]-Isopyrazam Spray Dilution 2 (0.31 g/L). The absorption profiles looked similar for all samples. 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 Isopyrazam from Spray Dilution 2 through human split thickness skin was <0.01 µg equiv./cm^2/h during the 24 h experimental period. The amount penetrated at 24 h, as measured in the receptor fluid, was 0.07 µg equiv./cm^2 (2.25% of the applied dose).

Following the skin wash at 6 h, 85.16% of the applied dose of Isopyrazam was washed off, with 8.11% removed with a skin wash at 24 h post dose. A proportion of the dose applied was recovered from the donor chamber (0.10%), 1.73% was found in the exposed skin and 0.07% was recovered from the receptor chamber wash. The mean total recovery was 99.36% of the applied dose.

The distribution of radioactivity (% applied dose) is provided in Table 28. The absorption profile is provided in Table 29 and Figure 22. The distribution by mass, of [^{14}C]-Isopyrazam at 24 h post dose is shown in Table 30. The absorption profile, by mass, is provided in Table 31 and Figure 23. The distribution of radioactivity in the stratum corneum, by mass, is provided in Table 32 and Figure 24.

5.0 CONCLUSIONS

The study demonstrated that the amount of Cyproconazole absorbed through human split-thickness skin membranes over 24 h (following a 6 h exposure) from the concentrate

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formulation (80 g/L), and the intended in-use concentrations, 0.8 g/L and 0.2 g/L, in Cyproconazole/Isopyrazam SC (A19022A) was 0.23%, 12.11% and 22.68% of the applied dose, respectively, as measured in the receptor fluid and receptor chamber wash.

The amount of Isopyrazam absorbed from the concentrate formulation (125 g/L), and the intended in-use concentrations, 1.25 g/L and 0.31 g/L, in Cyproconazole/Isopyrazam SC (A19022A) was 0.03%, 1.76% and 2.32% of the applied dose, respectively, as measured in the receptor fluid and receptor chamber wash.

6.0 REFERENCES

1. OECD Guideline for Testing of Chemicals, Guideline 428: Skin Absorption: *In Vitro* Method (2004).

2. OECD Environmental Health and Safety Publications Series on Testing and Assessment No. 28. Guidance Document for the Conduct of Skin Absorption Studies (2004).

3. European Commission Guidance Document on Dermal Absorption – Sanco/222/2000/Rev. 7 (19 March 2004).

4. Toner, F., (2011), Charles River Report No. 32053 'The *In Vitro* Absorption of Radiolabelled Caffeine and Testosterone Through Human Skin'.

5. Scientific Opinion on Dermal Absorption (EFSA Journal, 2012, 10(4): 2665).

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TABLE 1 Summary of Cyproconazole and Isopyrazam Distribution in the Test System

Test Preparation	Formulation Concentrate (80 g/L)	Spray Dilution 1 (0.8 g/L)	Spray Dilution 2 (0.2 g/L)	Formulation Concentrate (125 g/L)	Spray Dilution 1 (1.25 g/L)	Spray Dilution 2 (0.31g/L)
Test Item	Cyproconazole	Cyproconazole	Cyproconazole	Isopyrazam	Isopyrazam	Isopyrazam
Distribution	% Applied Dose	% Applied Dose	% Applied Dose	% Applied Dose	% Applied Dose	% Applied Dose
Donor Chamber Wash	0.03	0.05	0.04	0.01	0.10	0.10
Dislodgeable Dose 6 h*	99.98	85.63	73.97	96.11	85.58	85.16
Dislodgeable Dose 24 h*	0.58	2.48	2.37	0.20	7.26	8.11
Tape Strips 1-2	0.00	0.03	0.04	0.02	0.35	0.35
Tape Strips 3-20	0.00	0.09	0.15	0.03	1.70	1.51
Unexposed Skin	0.02	0.15	0.20	0.00	0.02	0.08
Exposed Skin	0.04	0.50	0.50	0.04	1.94	1.73
Receptor Fluid	0.22	11.88	22.05	0.03	1.72	2.25
Receptor Chamber Wash	0.01	0.23	0.62	0.00	0.04	0.07
Mass Balance	100.88	101.05	99.95	96.45	98.71	99.36
Distribution	µg equiv./cm^2	µg equiv./cm^2	µg equiv./cm^2	µg equiv./cm^2	µg equiv./cm^2	µg equiv./cm^2
Donor Chamber Wash	0.22	0.00	0.00	0.18	0.01	0.00
Dislodgeable Dose 6 h*	836.30	7.23	1.58	1184.71	11.34	2.80
Dislodgeable Dose 24 h*	4.84	0.21	0.05	2.47	0.96	0.27
Tape Strips 1-2	0.02	0.00	0.00	0.27	0.05	0.01
Tape Strips 3-20	0.08	0.07	0.00	0.37	0.22	0.05
Unexposed Skin	0.15	0.01	0.00	0.05	0.00	0.00
Exposed Skin	0.34	0.04	0.01	0.47	0.26	0.06
Receptor Fluid	1.81	1.00	0.47	0.33	0.23	0.07
Receptor Chamber Wash	0.08	0.02	0.01	0.03	0.01	0.00
Mass Balance	843.85	8.53	2.13	1188.87	13.08	3.27

* Dislodgeable Dose = Skin wash + Tissue swab + Pipette tip

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TABLE 2 Summary of Cyproconazole and Isopyrazam 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 ± SEM
(83.65 g/L Cyproconazole)	0-2	0.26 ± 0.11
10 µL/cm^2 (836.5 µg ai/cm^2)	2-6	0.09 ± 0.04
Unoccluded	6-24	0.06 ± 0.01
Duration of experiment: 24 h, n = 8	0-24	0.07 ± 0.01
Spray Dilution 1		µg equiv./cm^2/h ± SEM
(0.84 g/L Cyproconazole)	0-2	0.23 ± 0.03
10 µL/cm^2 (8.44 µg ai/cm^2)	2-6	0.04 ± 0.01
Unoccluded	6-24	0.02 ± 0.00
Duration of experiment: 24 h, n = 8	0-24	0.04 ± 0.00
Spray Dilution 2		µg equiv./cm^2/h ± SEM
(0. 21 g/L Cyproconazole)	0-2	0.13 ± 0.01
10 µL/cm^2 (2.13 µg ai/cm^2)	2-6	0.02 ± 0.01
Unoccluded	6-24	0.01 ± 0.00
Duration of experiment: 24 h, n = 8	0-24	0.02 ± 0.00
Formulation Concentrate		µg equiv./cm^2/h ± SEM
(123.26 g/L Isopyrazam)	0-2	0.01 ± 0.00
10 µL/cm^2 (1233 µg ai/cm^2)	2-6	0.03 ± 0.00
Unoccluded	6-24	0.01 ± 0.00
Duration of experiment: 24 h, n = 8	0-24	0.01 ± 0.00
Spray Dilution 1		µg equiv./cm^2/h ± SEM
(1.33 g/L Isopyrazam)	0-2	0.01 ± 0.00
10 µL/cm^2 (13.3 µg ai/cm^2)	2-6	0.01 ± 0.00
Unoccluded	6-24	0.01 ± 0.00
Duration of experiment: 24 h, n = 8	0-24	0.01 ± 0.00
Spray Dilution 2		µg equiv./cm^2/h ± SEM
(0.33 g/L Isopyrazam)	0-2	0.006 ± 0.001
10 µL/cm^2 (3.29 µg ai/cm^2)	2-6	0.004 ± 0.001
Unoccluded	6-24	0.003 ± 0.000
Duration of experiment: 24 h, n = 8	0-24	0.003 ± 0.000

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TABLE 3 Distribution of Radioactivity (% Applied Dose) at 24 h Post Dose Following Topical Application of [^{14}C]-Cyproconazole Formulation Concentrate (Test Preparation 1, 80 g/L) to Human Split-Thickness Membranes

	Cell Number and Donor Number									
	Cell 37 0403	Cell 38 0403	Cell 39 0410	Cell 40 0410	Cell 41 0401	Cell 42 0401	Cell 43 0444	Cell 44 0444	Mean	SD
Skin Wash 6 h	44.29	52.50	55.33	67.01	55.57	39.94	28.51	59.99	50.39	12.24
Tissue Swab 6 h	52.53	46.47	41.40	33.39	45.70	61.97	72.90	42.06	49.55	12.63
Pipette Tip 6 h	0.01	0.01	0.06	0.03	0.12	0.01	0.01	0.02	0.03	0.04
Skin Wash 24 h	2.39	0.29	0.05	0.04	0.05	0.09	*0.02	0.19	°0.39	°0.81
Tissue Swab 24 h	1.29	0.06	0.03	0.02	0.01	0.05	0.01	0.05	0.19	0.45
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	0.05	*0.01	0.13	*0.01	*0.00	*0.01	*0.01	*0.00	°0.03	°0.05
Stratum Corneum 1-2	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Stratum Corneum 3-5	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01
Stratum Corneum 6-10	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Stratum Corneum 11-15	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Stratum Corneum 16-20	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Unexposed Skin	0.01	*0.00	0.04	*0.00	0.01	*0.00	0.02	0.06	°0.02	°0.02
Exposed Skin	0.16	0.07	0.03	0.00	0.01	0.01	0.02	0.02	0.04	0.05
Receptor Fluid	0.29	0.27	0.23	0.12	0.13	0.10	0.31	0.27	0.22	0.09
Receptor Chamber Wash	*0.02	*0.01	*0.03	*0.01	*0.01	*0.00	*0.00	*0.01	°0.01	°0.01
Mass Balance	101.11	99.70	97.33	100.63	101.61	102.19	101.81	102.67	100.88	1.71

*=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

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TABLE 4 Cumulative Absorption (% Applied Dose) of [^{14}C]-Cyproconazole into Receptor Fluid Following Topical Application of the [^{14}C]-Cyproconazole Formulation Concentrate (Test Preparation 1, 80 g/L) to Human Split-Thickness Membranes

	Cell Number and Donor Number									
Time (h)	Cell 37 0403	Cell 38 0403	Cell 39 0410	Cell 40 0410	Cell 41 0401	Cell 42 0401	Cell 43 0444	Cell 44 0444	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	*0.03	0.04	*0.03	*0.01	0.14	0.18	°0.06	°0.06
4	0.06	0.05	0.05	0.05	*0.03	*0.03	0.17	0.15	°0.07	°0.05
6	0.13	0.12	0.10	0.06	*0.04	0.05	0.12	0.13	°0.09	°0.04
8	0.19	0.17	0.18	0.11	0.10	0.08	0.20	0.23	0.16	0.05
12	0.22	0.23	0.21	0.11	0.12	0.09	0.29	0.25	0.19	0.07
24	0.29	0.27	0.23	0.12	0.13	0.10	0.31	0.27	0.22	0.09

*=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

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TABLE 5 Distribution of Radioactivity (µg equiv./cm^2) at 24 h Post Dose Following Topical Application of [^{14}C]-Cyproconazole Formulation Concentrate (Test Preparation 1, 80 g/L) to Human Split-Thickness Membranes

	Cell Number and Donor Number									
	Cell 37 0403	Cell 38 0403	Cell 39 0410	Cell 40 0410	Cell 41 0401	Cell 42 0401	Cell 43 0444	Cell 44 0444	Mean	SD
Skin Wash 6 h	370.50	439.16	462.81	560.54	464.85	334.09	238.46	501.82	421.53	102.42
Tissue Swab 6 h	439.43	388.75	346.27	279.28	382.24	518.41	609.84	351.81	414.50	105.66
Pipette Tip 6 h	0.07	0.08	0.49	0.22	0.97	0.06	0.11	0.13	0.27	0.32
Skin Wash 24 h	19.96	2.40	0.46	0.33	0.42	0.76	*0.14	1.57	°3.25	°6.79
Tissue Swab 24 h	10.81	0.51	0.27	0.18	0.10	0.40	0.08	0.39	1.59	3.73
Pipette Tip 24 h	0.03	*0.00	*0.00	*0.00	*0.00	*0.00	*0.00	*0.00	°0.00	°0.01
Donor Chamber Wash	0.38	*0.05	1.11	*0.04	*0.03	*0.06	*0.04	*0.02	°0.22	°0.38
Stratum Corneum 1-2	0.09	0.03	0.02	0.00	0.01	0.02	0.01	0.01	0.02	0.03
Stratum Corneum 3-5	0.17	0.03	0.01	0.00	0.01	0.02	0.00	0.00	0.03	0.06
Stratum Corneum 6-10	0.11	0.02	0.01	0.01	0.01	0.01	0.00	0.01	0.02	0.04
Stratum Corneum 11-15	0.09	0.02	0.00	0.01	0.01	0.01	0.00	0.01	0.02	0.03
Stratum Corneum 16-20	0.05	0.02	0.00	0.00	0.00	0.00	0.00	0.01	0.01	0.02
Unexposed Skin	0.11	*0.01	0.31	*0.02	0.04	*0.03	0.15	0.53	°0.15	°0.18
Exposed Skin	1.34	0.55	0.28	*0.02	0.11	0.10	0.16	0.18	°0.34	°0.44
Receptor Fluid	2.46	2.29	1.88	1.03	1.10	0.80	2.59	2.30	1.81	0.72
Receptor Chamber Wash	*0.16	*0.06	*0.22	*0.05	*0.06	*0.02	*0.04	*0.06	°0.08	°0.07
Mass Balance	845.76	833.97	814.13	841.74	849.97	854.78	851.62	858.84	843.85	14.30

*=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

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TABLE 6 Cumulative Absorption (µg equiv./cm^2) of [^{14}C]-Cyproconazole into Receptor Fluid Following Topical Application of [^{14}C]-Cyproconazole Formulation Concentrate (Test Preparation 1, 80 g/L) to Human Split-Thickness Membranes

	Cell Number and Donor Number									
Time (h)	Cell 37 0403	Cell 38 0403	Cell 39 0410	Cell 40 0410	Cell 41 0401	Cell 42 0401	Cell 43 0444	Cell 44 0444	Mean	SD
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2	*0.13	*0.14	*0.28	0.37	*0.21	*0.06	1.17	1.50	°0.48	°0.54
4	0.50	0.43	0.45	0.41	*0.25	*0.26	1.40	1.24	°0.62	°0.45
6	1.05	1.02	0.85	0.54	*0.37	0.41	1.02	1.06	°0.79	°0.30
8	1.56	1.45	1.51	0.95	0.85	0.67	1.69	1.95	1.33	0.45
12	1.83	1.94	1.74	0.95	0.96	0.74	2.44	2.05	1.58	0.62
24	2.46	2.29	1.88	1.03	1.10	0.80	2.59	2.30	1.81	0.72

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TABLE 7 Distribution of Radioactivity (µg equiv./cm^2) in the Stratum Corneum at 24 h Post Dose Following Topical Application of [^{14}C]-Cyproconazole Formulation Concentrate (Test Preparation 1, 80 g/L) to Human Split-Thickness Membranes

	Distribution of Radioactivity at 24 h									
Tape Strip No.	Cell 37 0403	Cell 38 0403	Cell 39 0410	Cell 40 0410	Cell 41 0401	Cell 42 0401	Cell 43 0444	Cell 44 0444	Mean	SD
1	0.052	0.016	*0.005	*0.000	*0.005	*0.008	*0.001	*0.005	°0.012	°0.017
2	0.042	0.013	0.014	*0.002	*0.003	*0.008	*0.004	*0.004	°0.011	°0.013
3	0.069	0.014	*0.005	*0.001	*0.008	*0.007	*0.001	*0.001	°0.013	°0.023
4	0.065	*0.006	*0.003	*0.002	*0.001	*0.006	*0.002	*0.002	°0.011	°0.022
5	0.039	*0.007	*0.002	*0.001	*0.005	*0.004	*0.001	*0.001	°0.008	°0.013
6	0.044	*0.004	*0.002	*0.001	*0.001	*0.000	*0.000	*0.000	°0.006	°0.015
7	0.025	*0.004	*0.003	*0.001	*0.002	*0.000	*0.000	*0.001	°0.005	°0.008
8	0.013	*0.003	*0.000	*0.002	*0.001	*0.002	*0.000	*0.003	°0.003	°0.004
9	*0.010	*0.006	*0.004	*0.002	*0.003	*0.003	*0.002	*0.001	°0.004	°0.003
10	0.020	*0.004	*0.000	*0.003	*0.001	*0.003	*0.001	*0.002	°0.004	°0.006
11	0.021	*0.003	*0.000	*0.001	*0.000	*0.001	*0.001	*0.001	°0.004	°0.007
12	0.011	*0.006	*0.001	*0.003	*0.002	*0.003	*0.001	*0.001	°0.004	°0.004
13	0.021	*0.003	*0.000	*0.001	*0.003	*0.001	*0.001	*0.001	°0.004	°0.007
14	*0.009	*0.001	*0.000	*0.000	*0.002	*0.001	*0.001	*0.001	°0.002	°0.003
15	0.026	*0.003	*0.000	*0.001	*0.002	*0.002	*0.000	*0.002	°0.005	°0.009
16	0.018	*0.004	*0.001	*0.001	*0.000	*0.001	*0.003	*0.002	°0.004	°0.006
17	*0.009	*0.003	*0.000	*0.001	*0.001	*0.000	*0.000	*0.001	°0.002	°0.003
18	0.011	*0.004	*0.000	*0.001	*0.001	*0.001	*0.000	*0.001	°0.002	°0.004
19	*0.004	*0.003	*0.000	*0.000	*0.000	*0.000	*0.000	*0.001	°0.001	°0.002
20	0.012	*0.003	*0.001	*0.001	*0.000	*0.000	*0.001	*0.001	°0.002	°0.004

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TABLE 8 Distribution of Radioactivity (% Applied Dose) at 24 h Post Dose Following Topical Application of [^{14}C]-Cyproconazole Spray Dilution 1 (Test Preparation 2, 0.8 g/L) to Human Split-Thickness Membranes

	Cell Number and Donor Number									
	Cell 45 0403	Cell 46 0403	Cell 47 0410	Cell 48 0410	Cell 49 0401	Cell 50 0401	Cell 51 0444	Cell 52 0444	Mean	SD
Skin Wash 6 h	68.82	61.11	59.99	64.30	55.61	53.65	70.18	42.52	59.52	8.98
Tissue Swab 6 h	12.78	15.95	26.76	27.40	34.35	26.66	17.72	46.85	26.06	11.03
Pipette Tip 6 h	0.08	0.10	0.01	0.03	0.00	0.09	0.01	0.04	0.05	0.04
Skin Wash 24 h	2.85	6.29	0.48	0.57	2.12	2.38	1.27	0.22	2.02	1.98
Tissue Swab 24 h	1.21	0.96	0.27	0.12	0.27	0.54	0.24	0.09	0.46	0.41
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	0.03	0.03	0.13	0.12	0.03	0.07	*0.01	*0.01	°0.05	°0.05
Stratum Corneum 1-2	0.09	0.07	0.01	0.01	0.02	0.05	0.01	0.00	0.03	0.03
Stratum Corneum 3-5	0.03	0.05	0.01	0.00	0.02	0.04	0.01	0.01	0.02	0.02
Stratum Corneum 6-10	0.04	0.08	0.01	0.01	0.02	0.05	0.01	0.01	0.03	0.03
Stratum Corneum 11-15	0.05	0.05	0.00	0.00	0.02	0.03	0.01	0.00	0.02	0.02
Stratum Corneum 16-20	0.06	0.04	0.00	0.00	0.02	0.03	0.01	0.00	0.02	0.02
Unexposed Skin	0.06	0.03	0.32	0.51	0.03	0.18	0.06	0.02	0.15	0.18
Exposed Skin	0.80	1.22	0.27	0.20	0.40	0.75	0.15	0.23	0.50	0.38
Receptor Fluid	15.24	13.16	11.95	10.19	8.08	13.90	11.69	10.86	11.88	2.25
Receptor Chamber Wash	0.46	0.22	0.19	0.23	0.13	0.32	0.15	0.12	0.23	0.11
Mass Balance	102.59	99.36	100.39	103.71	101.13	98.72	101.52	100.97	101.05	1.62

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TABLE 9 Cumulative Absorption (% Applied Dose) of [^{14}C]-Cyproconazole into Receptor Fluid Following Topical Application of [^{14}C]-Cyproconazole Spray Dilution 1 (Test Preparation 2, 0.8 g/L) to Human Split-Thickness Membranes

	Cell Number and Donor Number									
Time (h)	Cell 45 0403	Cell 46 0403	Cell 47 0410	Cell 48 0410	Cell 49 0401	Cell 50 0401	Cell 51 0444	Cell 52 0444	Mean	SD
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2	5.76	3.10	10.13	8.35	2.73	5.21	6.74	6.04	6.01	2.48
4	7.90	5.22	11.21	8.59	4.23	6.61	9.08	7.70	7.57	2.21
6	9.80	7.57	11.44	9.27	4.78	8.40	9.14	7.29	8.46	1.98
8	11.64	9.65	12.11	10.28	7.14	12.11	11.31	9.21	10.43	1.72
12	12.47	11.42	12.02	10.22	7.87	14.83	11.51	10.07	11.30	2.03
24	15.24	13.16	11.95	10.19	8.08	13.90	11.69	10.86	11.88	2.25

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TABLE 10 Distribution of Radioactivity (µg equiv./cm^2) at 24 h Post Dose Following Topical Application of [^{14}C]-Cyproconazole Spray Dilution 1 (Test Preparation 2, 0.8 g/L) to Human Split-Thickness Membranes

	Cell Number and Donor Number									
	Cell 45 0403	Cell 46 0403	Cell 47 0410	Cell 48 0410	Cell 49 0401	Cell 50 0401	Cell 51 0444	Cell 52 0444	Mean	SD
Skin Wash 6 h	5.809	5.158	5.064	5.428	4.694	4.529	5.924	3.589	5.024	0.758
Tissue Swab 6 h	1.079	1.346	2.258	2.313	2.900	2.250	1.495	3.955	2.200	0.931
Pipette Tip 6 h	0.007	0.008	0.001	0.003	0.000	0.007	0.001	0.003	0.004	0.003
Skin Wash 24 h	0.241	0.531	0.040	0.048	0.179	0.201	0.108	0.018	0.171	0.167
Tissue Swab 24 h	0.102	0.081	0.023	0.010	0.023	0.045	0.020	0.008	0.039	0.035
Pipette Tip 24 h	0.000	0.000	*0.000	*0.000	0.000	0.000	*0.000	*0.000	°0.000	°0.000
Donor Chamber Wash	0.002	0.002	0.011	0.010	0.003	0.006	*0.001	*0.001	°0.004	°0.004
Stratum Corneum 1-2	0.007	0.006	0.001	0.001	0.002	0.004	0.001	0.000	0.003	0.003
Stratum Corneum 3-5	0.002	0.004	0.001	0.000	0.001	0.003	0.001	0.001	0.002	0.001
Stratum Corneum 6-10	0.004	0.007	0.001	0.001	0.002	0.004	0.001	0.001	0.002	0.002
Stratum Corneum 11-15	0.004	0.004	0.000	0.000	0.002	0.003	0.000	0.000	0.002	0.002
Stratum Corneum 16-20	0.005	0.003	0.000	0.000	0.002	0.002	0.001	0.000	0.002	0.002
Unexposed Skin	0.005	0.003	0.027	0.043	0.003	0.015	0.005	0.001	0.013	0.015
Exposed Skin	0.068	0.103	0.023	0.017	0.033	0.063	0.013	0.019	0.042	0.032
Receptor Fluid	1.286	1.111	1.008	0.860	0.682	1.173	0.986	0.916	1.003	0.190
Receptor Chamber Wash	0.039	0.019	0.016	0.020	0.011	0.027	0.013	0.010	0.019	0.010
Mass Balance	8.660	8.387	8.474	8.754	8.537	8.333	8.569	8.523	8.529	0.137

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TABLE 11 Cumulative Absorption (µg equiv./cm^2) of [^{14}C]-Cyproconazole into Receptor Fluid Following Topical Application of [^{14}C]-Cyproconazole Spray Dilution 1 (Test Preparation 2, 0.8 g/L) to Human Split-Thickness Membranes

	Cell Number and Donor Number									
Time (h)	Cell 45 0403	Cell 46 0403	Cell 47 0410	Cell 48 0410	Cell 49 0401	Cell 50 0401	Cell 51 0444	Cell 52 0444	Mean	SD
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2	0.49	0.26	0.86	0.71	0.23	0.44	0.57	0.51	0.51	0.21
4	0.67	0.44	0.95	0.73	0.36	0.56	0.77	0.65	0.64	0.19
6	0.83	0.64	0.97	0.78	0.40	0.71	0.77	0.62	0.71	0.17
8	0.98	0.81	1.02	0.87	0.60	1.02	0.95	0.78	0.88	0.15
12	1.05	0.96	1.01	0.86	0.66	1.25	0.97	0.85	0.95	0.17
24	1.29	1.11	1.01	0.86	0.68	1.17	0.99	0.92	1.00	0.19

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TABLE 12 Distribution of Radioactivity (µg equiv./cm^2) in the Stratum Corneum at 24 h Post Dose Following Topical Application of [^{14}C]-Cyproconazole Spray Dilution 1 (Test Preparation 2, 0.8 g/L) to Human Split-Thickness Membranes

	Distribution of Radioactivity at 24 h									
Tape Strip No.	Cell 45 0403	Cell 46 0403	Cell 47 0410	Cell 48 0410	Cell 49 0401	Cell 50 0401	Cell 51 0444	Cell 52 0444	Mean	SD
1	0.0047	0.0029	0.0005	0.0005	0.0015	0.0029	0.0003	0.0001	0.0017	0.0017
2	0.0027	0.0032	0.0003	0.0001	0.0005	0.0014	0.0003	0.0002	0.0011	0.0012
3	0.0009	0.0020	0.0007	*0.0001	0.0005	0.0012	0.0003	*0.0001	°0.0007	°0.0007
4	0.0009	0.0014	0.0001	0.0002	0.0005	0.0011	0.0002	0.0001	0.0006	0.0005
5	0.0003	0.0010	0.0001	0.0002	0.0003	0.0008	*0.0001	0.0004	°0.0004	°0.0003
6	0.0007	0.0023	0.0001	0.0001	0.0005	0.0010	0.0001	0.0003	0.0006	0.0007
7	0.0005	0.0009	0.0001	0.0002	0.0003	0.0010	0.0001	0.0001	0.0004	0.0004
8	0.0006	0.0011	0.0002	0.0001	0.0004	0.0007	0.0001	*0.0001	°0.0004	°0.0004
9	0.0007	0.0016	0.0001	0.0002	0.0004	0.0006	0.0001	0.0001	0.0005	0.0005
10	0.0012	0.0010	0.0001	0.0001	0.0005	0.0005	0.0002	*0.0001	°0.0005	°0.0004
11	0.0007	0.0010	*0.0000	0.0001	0.0003	0.0007	0.0001	*0.0001	°0.0004	°0.0004
12	0.0008	0.0010	0.0001	*0.0001	0.0005	0.0006	*0.0001	*0.0001	°0.0004	°0.0004
13	0.0005	0.0008	0.0001	*0.0000	0.0004	0.0005	*0.0001	*0.0001	°0.0003	°0.0003
14	0.0008	0.0007	0.0001	*0.0001	0.0003	0.0006	0.0001	*0.0001	°0.0003	°0.0003
15	0.0011	0.0008	*0.0001	0.0001	0.0003	0.0004	0.0001	*0.0000	°0.0004	°0.0004
16	0.0009	0.0007	*0.0001	*0.0000	0.0003	0.0006	0.0001	*0.0000	°0.0003	°0.0003
17	0.0006	0.0008	*0.0001	*0.0001	0.0003	0.0004	0.0001	*0.0000	°0.0003	°0.0003
18	0.0010	0.0006	*0.0000	*0.0001	0.0003	0.0005	*0.0001	*0.0000	°0.0003	°0.0004
19	0.0015	0.0005	*0.0000	0.0001	0.0003	0.0004	*0.0000	*0.0000	°0.0004	°0.0005
20	0.0012	0.0005	*0.0000	0.0001	0.0005	0.0005	0.0002	*0.0000	°0.0004	°0.0004

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TABLE 13 Distribution of Radioactivity (% Applied Dose) at 24 h Post Dose Following Topical Application of [^{14}C]-Cyproconazole Spray Dilution 2 (Test Preparation 3, 0.2 g/L) to Human Split-Thickness Membranes

	Cell Number and Donor Number									
	Cell 53 0403	Cell 54 0403	Cell 55 0410	Cell 56 0410	Cell 57 0401	Cell 58 0401	Cell 59 0444	Cell 60 0444	Mean	SD
Skin Wash 6 h	53.29	58.77	51.88	54.93	63.22	50.59	49.88	50.71	54.16	4.67
Tissue Swab 6 h	20.67	20.28	24.52	25.79	11.80	19.85	16.60	18.69	19.78	4.39
Pipette Tip 6 h	0.03	0.01	0.02	0.01	0.15	0.02	0.07	0.01	0.04	0.05
Skin Wash 24 h	3.11	1.49	3.24	0.85	2.23	2.13	0.36	0.66	1.76	1.10
Tissue Swab 24 h	0.87	0.65	1.05	0.25	0.66	0.75	0.23	0.40	0.61	0.29
Pipette Tip 24 h	*0.00	*0.00	*0.00	*0.00	0.01	0.00	*0.00	*0.00	°0.00	°0.00
Donor Chamber Wash	*0.07	0.21	*0.03	*0.00	*0.01	*0.02	*0.01	*0.01	°0.04	°0.07
Stratum Corneum 1-2	0.06	0.11	0.05	0.01	0.04	0.06	0.01	0.02	0.04	0.03
Stratum Corneum 3-5	0.05	0.06	0.03	0.02	0.05	0.05	0.01	0.01	0.04	0.02
Stratum Corneum 6-10	0.06	0.10	0.03	0.01	0.06	0.06	0.01	0.01	0.04	0.03
Stratum Corneum 11-15	0.12	0.03	0.02	0.01	0.05	0.05	0.01	0.00	0.04	0.04
Stratum Corneum 16-20	0.07	0.02	0.02	0.01	0.05	0.03	0.00	0.00	0.03	0.02
Unexposed Skin	0.68	0.23	0.13	0.08	0.07	0.24	0.06	0.13	0.20	0.21
Exposed Skin	0.22	0.72	0.51	0.25	0.58	0.74	0.46	0.50	0.50	0.19
Receptor Fluid	19.34	17.63	18.38	17.33	20.24	25.35	30.16	28.00	22.05	5.04
Receptor Chamber Wash	0.55	0.29	0.76	0.60	0.44	0.74	0.94	0.65	0.62	0.20
Mass Balance	99.20	100.60	100.68	100.18	99.64	100.71	98.80	99.80	99.95	0.71

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TABLE 14 Cumulative Absorption (% Applied Dose) of [^{14}C]-Cyproconazole into Receptor Fluid Following Topical Application of the [^{14}C]-Cyproconazole Spray Dilution 2 (Test Preparation 3, 0.2 g/L) to Human Split-Thickness Membranes

	Cell Number and Donor Number									
Time (h)	Cell 53 0403	Cell 54 0403	Cell 55 0410	Cell 56 0410	Cell 57 0401	Cell 58 0401	Cell 59 0444	Cell 60 0444	Mean	SD
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2	10.07	7.87	12.33	14.98	10.84	9.05	16.77	14.89	12.10	3.18
4	12.81	12.36	14.44	16.45	10.42	17.18	18.31	15.72	14.71	2.69
6	15.09	14.36	16.21	17.15	13.77	19.95	17.84	16.81	16.40	2.01
8	18.17	16.34	17.76	17.95	18.88	24.28	28.16	26.15	20.96	4.51
12	18.90	17.58	18.24	17.82	19.84	24.91	32.05	28.12	22.18	5.50
24	19.34	17.63	18.38	17.33	20.24	25.35	30.16	28.00	22.05	5.04

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TABLE 15 Distribution of Radioactivity (µg equiv./cm^2) at 24 h Post Dose Following Topical Application of [^{14}C]-Cyproconazole Spray Dilution 2 (Test Preparation 3, 0.2 g/L) to Human Split-Thickness Membranes

	Cell Number and Donor Number									
	Cell 53 0403	Cell 54 0403	Cell 55 0410	Cell 56 0410	Cell 57 0401	Cell 58 0401	Cell 59 0444	Cell 60 0444	Mean	SD
Skin Wash 6 h	1.137	1.254	1.107	1.172	1.349	1.080	1.064	1.082	1.156	0.100
Tissue Swab 6 h	0.441	0.433	0.523	0.550	0.252	0.424	0.354	0.399	0.422	0.094
Pipette Tip 6 h	0.001	0.000	0.001	0.000	0.003	0.000	0.001	0.000	0.001	0.001
Skin Wash 24 h	0.066	0.032	0.069	0.018	0.047	0.046	0.008	0.014	0.038	0.023
Tissue Swab 24 h	0.019	0.014	0.022	0.005	0.014	0.016	0.005	0.008	0.013	0.006
Pipette Tip 24 h	*0.000	*0.000	*0.000	*0.000	0.000	0.000	*0.000	*0.000	°0.000	°0.000
Donor Chamber Wash	*0.001	0.004	*0.001	*0.000	*0.000	*0.000	*0.000	*0.000	°0.001	°0.001
Stratum Corneum 1-2	0.001	0.002	0.001	0.000	0.001	0.001	0.000	0.000	0.001	0.001
Stratum Corneum 3-5	0.001	0.001	0.001	0.000	0.001	0.001	0.000	0.000	0.001	0.000
Stratum Corneum 6-10	0.001	0.002	0.001	0.000	0.001	0.001	0.000	0.000	0.001	0.001
Stratum Corneum 11-15	0.003	0.001	0.000	0.000	0.001	0.001	0.000	0.000	0.001	0.001
Stratum Corneum 16-20	0.002	0.000	0.001	0.000	0.001	0.001	0.000	0.000	0.001	0.001
Unexposed Skin	0.015	0.005	0.003	0.002	0.002	0.005	0.001	0.003	0.004	0.004
Exposed Skin	0.005	0.015	0.011	0.005	0.012	0.016	0.010	0.011	0.011	0.004
Receptor Fluid	0.412	0.376	0.391	0.369	0.431	0.540	0.642	0.596	0.470	0.107
Receptor Chamber Wash	0.012	0.006	0.016	0.013	0.009	0.016	0.020	0.014	0.013	0.004
Mass Balance	2.116	2.146	2.148	2.137	2.126	2.148	2.107	2.129	2.132	0.015

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TABLE 16 Cumulative Absorption (µg equiv./cm^2) of [^{14}C]-Cyproconazole into Receptor Fluid Following Topical Application of [^{14}C]-Cyproconazole Spray Dilution 2 (Test Preparation 3, 0.2 g/L) to Human Split-Thickness Membranes

	Cell Number and Donor Number									
Time (h)	Cell 53 0403	Cell 54 0403	Cell 55 0410	Cell 56 0410	Cell 57 0401	Cell 58 0401	Cell 59 0444	Cell 60 0444	Mean	SD
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2	0.21	0.17	0.26	0.32	0.23	0.19	0.36	0.32	0.26	0.07
4	0.27	0.26	0.31	0.35	0.22	0.37	0.39	0.33	0.31	0.06
6	0.32	0.31	0.35	0.37	0.29	0.42	0.38	0.36	0.35	0.04
8	0.39	0.35	0.38	0.38	0.40	0.52	0.60	0.56	0.45	0.10
12	0.40	0.37	0.39	0.38	0.42	0.53	0.68	0.60	0.47	0.12
24	0.41	0.38	0.39	0.37	0.43	0.54	0.64	0.60	0.47	0.11

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TABLE 17 Distribution of Radioactivity (µg equiv./cm^2) in the Stratum Corneum at 24 h Post Dose Following Topical Application of [^{14}C]-Cyproconazole Spray Dilution 2 (Test Preparation 3, 0.2 g/L) to Human Split-Thickness Membranes

	Distribution of Radioactivity at 24 h									
Tape Strip No.	Cell 53 0403	Cell 54 0403	Cell 55 0410	Cell 56 0410	Cell 57 0401	Cell 58 0401	Cell 59 0444	Cell 60 0444	Mean	SD
1	0.0006	0.0011	0.0006	0.0002	0.0006	0.0009	*0.0001	0.0003	°0.0005	°0.0003
2	0.0006	0.0012	0.0004	0.0001	0.0003	0.0005	0.0001	0.0001	0.0004	0.0004
3	0.0005	0.0005	0.0002	0.0001	0.0006	0.0003	0.0001	*0.0001	°0.0003	°0.0002
4	0.0004	0.0004	0.0002	0.0001	0.0002	0.0002	0.0001	*0.0001	°0.0002	°0.0001
5	0.0003	0.0004	0.0002	0.0002	0.0003	0.0007	0.0001	0.0001	0.0003	0.0002
6	0.0005	0.0004	0.0001	*0.0001	0.0001	0.0004	*0.0001	*0.0000	°0.0002	°0.0002
7	0.0003	0.0007	0.0001	*0.0001	0.0004	0.0001	*0.0000	*0.0000	°0.0002	°0.0002
8	0.0003	0.0006	0.0001	*0.0001	0.0001	0.0002	*0.0000	*0.0000	°0.0002	°0.0002
9	0.0002	0.0003	0.0001	*0.0000	0.0003	0.0002	*0.0001	*0.0000	°0.0002	°0.0001
10	0.0001	0.0002	0.0001	*0.0001	0.0003	0.0002	*0.0001	*0.0000	°0.0001	°0.0001
11	0.0002	0.0002	0.0001	0.0001	0.0001	0.0003	*0.0000	*0.0000	°0.0001	°0.0001
12	0.0004	0.0002	0.0001	*0.0001	0.0002	0.0002	*0.0000	*0.0000	°0.0001	°0.0001
13	0.0008	0.0001	0.0001	*0.0000	0.0002	0.0002	*0.0000	*0.0000	°0.0002	°0.0003
14	0.0007	0.0001	0.0001	*0.0000	0.0002	0.0002	*0.0000	*0.0000	°0.0002	°0.0002
15	0.0005	0.0002	*0.0001	*0.0000	0.0004	0.0003	*0.0000	*0.0000	°0.0002	°0.0002
16	0.0005	0.0001	0.0001	*0.0000	0.0002	0.0002	*0.0000	*0.0000	°0.0002	°0.0002
17	0.0002	*0.0001	0.0001	*0.0000	0.0002	0.0001	*0.0000	*0.0000	°0.0001	°0.0001
18	0.0002	*0.0001	*0.0001	*0.0000	0.0001	0.0001	*0.0000	*0.0000	°0.0001	°0.0001
19	0.0003	0.0001	0.0001	*0.0000	0.0002	0.0001	*0.0000	*0.0000	°0.0001	°0.0001
20	0.0003	*0.0001	0.0001	*0.0000	0.0002	0.0002	*0.0000	*0.0000	°0.0001	°0.0001

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TABLE 18 Distribution of Radioactivity (% Applied Dose) at 24 h Post Dose Following Topical Application of [^{14}C]-Isopyrazam Formulation Concentrate (Test Preparation 4, 125 g/L) to Human Split-Thickness Membranes

	Cell Number and Donor Number									
	Cell 61 0401	Cell 62 0401	Cell 63 0410	Cell 64 0410	Cell 65 0420	Cell 66 0420	Cell 67 0445	Cell 68 0445	Mean	SD
Skin Wash 6 h	61.40	69.63	52.04	67.22	59.13	52.34	41.89	49.57	56.65	9.39
Tissue Swab 6 h	33.71	29.98	40.83	32.07	37.07	45.81	53.51	42.40	39.42	7.85
Pipette Tip 6 h	0.08	0.02	0.02	0.06	0.04	0.02	0.03	0.04	0.04	0.02
Skin Wash 24 h	0.05	0.10	0.06	0.12	0.32	0.11	0.17	0.16	0.14	0.09
Tissue Swab 24 h	0.01	0.06	0.03	0.05	0.16	0.04	0.11	0.06	0.06	0.05
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	*0.00	*0.01	*0.01	*0.05	*0.01	*0.00	*0.03	*0.01	°0.01	°0.02
Stratum Corneum 1-2	0.02	0.01	0.01	0.02	0.03	0.01	0.08	0.00	0.02	0.03
Stratum Corneum 3-5	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.00
Stratum Corneum 6-10	0.00	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.00
Stratum Corneum 11-15	0.00	0.00	0.00	0.01	0.01	0.01	0.01	0.01	0.01	0.00
Stratum Corneum 16-20	0.00	0.00	0.00	0.00	0.01	0.00	0.01	0.00	0.00	0.00
Unexposed Skin	*0.00	*0.00	*0.00	0.02	*0.00	*0.00	*0.00	*0.00	°0.00	°0.01
Exposed Skin	0.03	0.01	0.02	0.02	0.04	0.02	0.11	0.05	0.04	0.03
Receptor Fluid	*0.02	*0.02	*0.01	*0.03	*0.03	*0.02	*0.05	*0.03	°0.03	°0.01
Receptor Chamber Wash	*0.00	*0.00	*0.00	*0.02	*0.00	*0.00	*0.00	*0.00	°0.00	°0.01
Mass Balance	95.34	99.84	93.06	99.71	96.87	98.40	96.03	92.36	96.45	2.82

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TABLE 19 Cumulative Absorption (% Applied Dose) of [^{14}C]-Isopyrazam into Receptor Fluid Following Topical Application of [^{14}C]-Isopyrazam Formulation Concentrate (Test Preparation 4, 125 g/L) to Human Split-Thickness Membranes

	Cell Number and Donor Number									
Time (h)	Cell 61 0401	Cell 62 0401	Cell 63 0410	Cell 64 0410	Cell 65 0420	Cell 66 0420	Cell 67 0445	Cell 68 0445	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	*0.00	*0.00	*0.00	*0.00	*0.00	*0.00	°0.00	°0.00
4	*0.00	*0.01	*0.01	*0.01	*0.01	*0.01	*0.01	*0.01	°0.01	°0.00
6	*0.01	*0.00	*0.01	*0.01	*0.01	*0.01	*0.02	*0.01	°0.01	°0.00
8	*0.01	*0.01	*0.01	*0.01	*0.01	*0.01	*0.02	*0.01	°0.01	°0.00
12	*0.01	*0.01	*0.01	*0.01	*0.01	*0.01	*0.03	*0.01	°0.01	°0.01
24	*0.02	*0.02	*0.01	*0.03	*0.03	*0.02	0.05	*0.03	°0.03	°0.01

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TABLE 20 Distribution of Radioactivity (µg equiv./cm^2) at 24 h Post Dose Following Topical Application of [^{14}C]-Isopyrazam Formulation Concentrate (Test Preparation 4, 125 g/L) to Human Split-Thickness Membranes

	Cell Number and Donor Number									
	Cell 61 0401	Cell 62 0401	Cell 63 0410	Cell 64 0410	Cell 65 0420	Cell 66 0420	Cell 67 0445	Cell 68 0445	Mean	SD
Skin Wash 6 h	756.80	858.28	641.46	828.51	728.81	645.18	516.37	611.03	698.31	115.68
Tissue Swab 6 h	415.54	369.53	503.27	395.36	456.98	564.72	659.55	522.61	485.94	96.76
Pipette Tip 6 h	0.99	0.26	0.21	0.71	0.44	0.21	0.35	0.49	0.46	0.27
Skin Wash 24 h	0.59	1.22	0.77	1.46	3.95	1.30	2.10	2.01	1.68	1.06
Tissue Swab 24 h	0.14	0.70	0.32	0.66	1.99	0.44	1.31	0.79	0.79	0.60
Pipette Tip 24 h	*0.00	*0.00	*0.00	*0.00	*0.00	*0.00	*0.01	*0.01	°0.00	°0.00
Donor Chamber Wash	*0.01	*0.07	*0.12	*0.61	*0.07	*0.00	*0.41	*0.14	°0.18	°0.22
Stratum Corneum 1-2	0.22	0.09	0.13	0.19	0.35	0.09	1.01	0.05	0.27	0.31
Stratum Corneum 3-5	0.12	0.07	0.12	0.12	0.17	0.13	0.17	0.07	0.12	0.04
Stratum Corneum 6-10	0.04	0.06	0.06	0.11	0.18	0.16	0.15	0.09	0.11	0.05
Stratum Corneum 11-15	0.05	0.03	0.05	0.07	0.13	0.10	0.12	0.06	0.08	0.04
Stratum Corneum 16-20	0.04	0.02	0.02	0.05	0.11	0.04	0.14	0.06	0.06	0.04
Unexposed Skin	*0.01	*0.04	*0.03	0.30	*0.01	*0.01	*0.01	*0.01	°0.05	°0.10
Exposed Skin	0.35	0.12	0.30	0.23	0.51	0.24	1.36	0.66	0.47	0.40
Receptor Fluid	*0.27	*0.21	*0.18	*0.40	*0.31	*0.26	*0.65	*0.34	°0.33	°0.15
Receptor Chamber Wash	*0.00	*0.00	*0.00	*0.19	*0.02	*0.00	*0.00	*0.00	°0.03	°0.07
Mass Balance	1175.18	1230.69	1147.05	1228.97	1194.04	1212.87	1183.70	1138.44	1188.87	34.78

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TABLE 21 Cumulative Absorption (µg equiv./cm^2) of [^{14}C]-Isopyrazam into Receptor Fluid Following Topical Application of [^{14}C]-Isopyrazam Formulation Concentrate (Test Preparation 4, 125 g/L) to Human Split-Thickness Membranes

	Cell Number and Donor Number									
	Cell 61	Cell 62	Cell 63	Cell 64	Cell 65	Cell 66	Cell 67	Cell 68		
Time (h)	0401	0401	0410	0410	0420	0420	0445	0445	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	*0.02	*0.01	*0.01	*0.02	*0.00	*0.00	°0.01	°0.01
4	*0.00	*0.10	*0.08	*0.08	*0.08	*0.12	*0.16	*0.11	°0.09	°0.04
6	*0.13	*0.04	*0.11	*0.08	*0.10	*0.13	*0.19	*0.17	°0.12	°0.05
8	*0.17	*0.14	*0.13	*0.15	*0.18	*0.18	*0.29	*0.18	°0.18	°0.05
12	*0.10	*0.13	*0.11	*0.18	*0.18	*0.10	*0.36	*0.17	°0.16	°0.09
24	*0.27	*0.21	*0.18	*0.40	*0.31	*0.26	0.65	*0.34	°0.33	°0.15

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TABLE 22 Distribution of Radioactivity (µg equiv./cm^2) in the Stratum Corneum at 24 h Post Dose Following Topical Application of [^{14}C]-Isopyrazam Formulation Concentrate (Test Preparation 4, 125 g/L) to Human Split-Thickness Membranes

	Distribution of Radioactivity at 24 h									
Tape Strip No.	Cell 61 0401	Cell 62 0401	Cell 63 0410	Cell 64 0410	Cell 65 0420	Cell 66 0420	Cell 67 0445	Cell 68 0445	Mean	SD
1	0.1997	0.0506	0.0583	0.1407	0.1823	0.0429	0.8468	0.0198	0.1926	0.2729
2	0.0202	0.0407	0.0682	0.0538	0.1705	0.0469	0.1614	0.0318	0.0742	0.0585
3	0.0355	0.0311	0.0253	0.0513	0.0761	0.0349	0.0369	0.0205	0.0390	0.0175
4	0.0607	0.0201	0.0273	0.0371	0.0528	0.0484	0.0968	0.0325	0.0470	0.0243
5	0.0250	0.0192	0.0676	0.0291	0.0398	0.0504	0.0332	0.0214	0.0357	0.0164
6	*0.0122	0.0207	0.0214	0.0313	0.0775	0.0650	0.0338	0.0213	°0.0354	°0.0234
7	*0.0096	*0.0124	*0.0131	0.0226	0.0361	0.0380	0.0257	0.0291	°0.0233	°0.0109
8	*0.0067	0.0204	*0.0091	0.0227	0.0176	0.0233	0.0218	0.0196	°0.0176	°0.0063
9	*0.0018	*0.0058	*0.0146	*0.0130	0.0255	*0.0098	0.0474	*0.0095	°0.0159	°0.0145
10	*0.0109	*0.0049	*0.0065	0.0208	0.0219	0.0221	0.0192	*0.0138	°0.0150	°0.0070
11	*0.0153	*0.0061	*0.0114	0.0213	0.0470	0.0209	0.0187	0.0200	°0.0201	°0.0121
12	*0.0109	*0.0020	*0.0040	*0.0123	0.0178	*0.0137	0.0330	*0.0137	°0.0134	°0.0095
13	*0.0111	*0.0088	*0.0115	*0.0155	*0.0110	0.0425	0.0239	*0.0119	°0.0170	°0.0113
14	*0.0038	*0.0082	*0.0077	*0.0130	0.0330	*0.0128	0.0181	*0.0090	°0.0132	°0.0091
15	*0.0075	*0.0036	*0.0117	*0.0098	0.0251	*0.0088	0.0234	*0.0100	°0.0125	°0.0076
16	*0.0088	*0.0060	*0.0036	*0.0137	0.0466	*0.0080	0.0388	0.0171	°0.0178	°0.0160
17	*0.0054	*0.0049	*0.0060	*0.0087	*0.0136	*0.0086	0.0338	*0.0143	°0.0119	°0.0095
18	*0.0089	*0.0024	*0.0080	*0.0063	*0.0114	*0.0097	0.0173	*0.0077	°0.0090	°0.0043
19	*0.0022	*0.0003	*0.0027	*0.0091	0.0223	*0.0066	0.0179	*0.0055	°0.0083	°0.0078
20	0.0194	*0.0023	*0.0039	*0.0080	*0.0120	*0.0033	0.0289	*0.0157	°0.0117	°0.0093

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TABLE 23 Distribution of Radioactivity (% Applied Dose) at 24 h Post Dose Following Topical Application of [^{14}C]-Isopyrazam Spray Dilution 1 (Test Preparation 5, 1.25 g/L) to Human Split-Thickness Membranes

	Cell Number and Donor Number									
	Cell 69 0401	Cell 70 0401	Cell 71 0410	Cell 72 0410	Cell 73 0420	Cell 74 0420	Cell 75 0445	Cell 76 0445	Mean	SD
Skin Wash 6 h	53.97	54.86	64.10	75.01	61.89	61.30	56.90	52.76	60.10	7.29
Tissue Swab 6 h	34.01	29.39	16.06	17.34	26.37	21.63	24.99	33.36	25.39	6.77
Pipette Tip 6 h	0.14	0.08	0.14	0.03	0.05	0.07	0.09	0.05	0.08	0.04
Skin Wash 24 h	4.47	4.46	8.44	3.51	3.89	6.99	6.29	4.22	5.28	1.75
Tissue Swab 24 h	1.89	1.20	3.69	1.08	0.98	2.63	2.99	1.27	1.97	1.02
Pipette Tip 24 h	0.00	0.00	0.02	0.00	0.01	0.00	0.01	0.02	0.01	0.01
Donor Chamber Wash	0.12	0.22	0.21	0.03	*0.02	*0.01	0.15	0.05	°0.10	°0.08
Stratum Corneum 1-2	0.27	0.21	0.78	0.07	0.33	0.74	0.17	0.27	0.35	0.26
Stratum Corneum 3-5	0.21	0.28	0.93	0.19	0.57	0.87	0.16	0.38	0.45	0.31
Stratum Corneum 6-10	0.28	0.59	0.59	0.27	0.64	0.81	0.22	0.41	0.47	0.21
Stratum Corneum 11-15	0.33	0.52	0.18	0.26	0.32	1.18	0.19	0.32	0.41	0.33
Stratum Corneum 16-20	0.26	0.42	0.07	0.24	1.12	0.31	0.24	0.22	0.36	0.32
Unexposed Skin	0.01	0.01	0.02	*0.00	0.00	0.00	0.09	0.03	°0.02	°0.03
Exposed Skin	0.98	3.32	0.52	0.95	1.57	1.00	4.21	2.96	1.94	1.37
Receptor Fluid	*2.33	*1.77	*1.84	*0.53	*0.81	*1.01	*2.93	*2.53	°1.72	°0.87
Receptor Chamber Wash	0.04	0.03	0.10	*0.01	0.02	0.04	0.06	0.05	°0.04	°0.03
Mass Balance	99.32	97.38	97.68	99.52	98.57	98.59	99.70	98.90	98.71	0.84

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TABLE 24 Cumulative Absorption (% Applied Dose) of [^{14}C]-Isopyrazam into Receptor Fluid Following Topical Application of [^{14}C]-Isopyrazam Spray Dilution 1 (Test Preparation 5, 1.25 g/L) to Human Split-Thickness Membranes

	Cell Number and Donor Number									
Time (h)	Cell 69 0401	Cell 70 0401	Cell 71 0410	Cell 72 0410	Cell 73 0420	Cell 74 0420	Cell 75 0445	Cell 76 0445	Mean	SD
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2	0.26	0.13	0.20	0.12	0.07	0.17	0.09	0.06	0.14	0.07
4	0.68	0.27	0.33	0.19	0.21	0.31	0.26	0.09	0.29	0.18
6	1.19	0.40	0.50	0.25	0.27	0.38	0.37	0.16	0.44	0.32
8	1.55	0.75	0.63	0.30	0.46	0.55	0.58	0.20	0.63	0.41
12	1.82	1.09	1.14	0.40	0.63	0.75	1.67	0.99	1.06	0.49
24	2.33	1.77	1.84	0.53	0.81	1.01	2.93	2.53	1.72	0.87

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TABLE 25 Distribution of Radioactivity (µg equiv./cm^2) at 24 h Post Dose Following Topical Application of [^{14}C]-Isopyrazam Spray Dilution 1 (Test Preparation 5, 1.25 g/L) to Human Split-Thickness Membranes

	Cell Number and Donor Number									
	Cell 69 0401	Cell 70 0401	Cell 71 0410	Cell 72 0410	Cell 73 0420	Cell 74 0420	Cell 75 0445	Cell 76 0445	Mean	SD
Skin Wash 6 h	7.152	7.270	8.493	9.940	8.201	8.123	7.540	6.991	7.964	0.966
Tissue Swab 6 h	4.506	3.894	2.128	2.298	3.493	2.866	3.311	4.421	3.365	0.897
Pipette Tip 6 h	0.019	0.011	0.018	0.004	0.006	0.009	0.013	0.007	0.011	0.005
Skin Wash 24 h	0.592	0.591	1.119	0.465	0.516	0.926	0.834	0.559	0.700	0.232
Tissue Swab 24 h	0.251	0.159	0.489	0.143	0.130	0.349	0.396	0.168	0.261	0.135
Pipette Tip 24 h	0.000	0.000	0.002	0.000	0.001	0.001	0.001	0.003	0.001	0.001
Donor Chamber Wash	0.016	0.029	0.028	0.004	*0.002	*0.001	0.020	0.006	°0.013	°0.011
Stratum Corneum 1-2	0.036	0.028	0.104	0.009	0.043	0.097	0.022	0.035	0.047	0.035
Stratum Corneum 3-5	0.028	0.038	0.124	0.026	0.076	0.115	0.021	0.051	0.060	0.041
Stratum Corneum 6-10	0.037	0.078	0.078	0.035	0.084	0.108	0.029	0.054	0.063	0.028
Stratum Corneum 11-15	0.043	0.069	0.024	0.035	0.042	0.157	0.025	0.043	0.055	0.044
Stratum Corneum 16-20	0.035	0.056	0.009	0.031	0.149	0.042	0.032	0.029	0.048	0.043
Unexposed Skin	0.002	0.002	0.002	*0.000	0.000	0.000	0.012	0.004	°0.003	°0.004
Exposed Skin	0.129	0.440	0.068	0.126	0.207	0.132	0.558	0.393	0.257	0.181
Receptor Fluid	*0.309	*0.235	*0.243	*0.070	*0.107	*0.134	*0.389	*0.335	°0.228	°0.115
Receptor Chamber Wash	0.006	0.004	0.013	*0.001	0.003	0.005	0.008	0.006	°0.006	°0.004
Mass Balance	13.160	12.903	12.943	13.187	13.061	13.064	13.211	13.104	13.079	0.111

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TABLE 26 Cumulative Absorption (µg equiv./cm^2) of [^{14}C]-Isopyrazam into Receptor Fluid Following Topical Application of [^{14}C]-Isopyrazam Spray Dilution 1 (Test Preparation 5, 1.25 g/L) to Human Split-Thickness Membranes

	Cell Number and Donor Number									
	Cell 69	Cell 70	Cell 71	Cell 72	Cell 73	Cell 74	Cell 75	Cell 76		
Time (h)	0401	0401	0410	0410	0420	0420	0445	0445	Mean	SD
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2	0.03	0.02	0.03	0.02	0.01	0.02	0.01	0.01	0.02	0.01
4	0.09	0.04	0.04	0.03	0.03	0.04	0.03	0.01	0.04	0.02
6	0.16	0.05	0.07	0.03	0.04	0.05	0.05	0.02	0.06	0.04
8	0.21	0.10	0.08	0.04	0.06	0.07	0.08	0.03	0.08	0.05
12	0.24	0.14	0.15	0.05	0.08	0.10	0.22	0.13	0.14	0.07
24	0.31	0.24	0.24	0.07	0.11	0.13	0.39	0.34	0.23	0.12

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TABLE 27 Distribution of Radioactivity (µg equiv./cm^2) in the Stratum Corneum at 24 h Post Dose Following Topical Application of [^{14}C]-Isopyrazam Spray Dilution 1 (Test Preparation 5, 1.25 g/L) to Human Split-Thickness Membranes

	Distribution of Radioactivity at 24 h									
Tape Strip No.	Cell 69 0401	Cell 70 0401	Cell 71 0410	Cell 72 0410	Cell 73 0420	Cell 74 0420	Cell 75 0445	Cell 76 0445	Mean	SD
1	0.0219	0.0180	0.0475	0.0033	0.0301	0.0381	0.0140	0.0192	0.0240	0.0140
2	0.0137	0.0103	0.0562	0.0056	0.0133	0.0594	0.0081	0.0161	0.0228	0.0218
3	0.0096	0.0084	0.0654	0.0084	0.0360	0.0436	0.0086	0.0141	0.0243	0.0216
4	0.0059	0.0201	0.0423	0.0058	0.0203	0.0464	0.0070	0.0156	0.0204	0.0160
5	0.0127	0.0090	0.0161	0.0116	0.0198	0.0249	0.0053	0.0210	0.0150	0.0066
6	0.0133	0.0149	0.0267	0.0115	0.0258	0.0271	0.0068	0.0159	0.0178	0.0078
7	0.0057	0.0081	0.0160	0.0058	0.0132	0.0463	0.0061	0.0077	0.0136	0.0137
8	0.0033	0.0084	0.0049	0.0053	0.0115	0.0106	0.0039	0.0114	0.0074	0.0035
9	0.0093	0.0308	0.0213	0.0067	0.0088	0.0112	0.0054	0.0111	0.0131	0.0086
10	0.0056	0.0159	0.0094	0.0062	0.0251	0.0125	0.0063	0.0075	0.0111	0.0067
11	0.0130	0.0167	0.0067	0.0077	0.0090	0.0181	0.0051	0.0130	0.0112	0.0048
12	0.0049	0.0062	0.0071	0.0018	0.0096	0.0205	0.0024	0.0059	0.0073	0.0059
13	0.0071	0.0113	0.0026	0.0053	0.0047	0.0327	0.0072	0.0097	0.0101	0.0095
14	0.0091	0.0176	0.0045	0.0072	0.0087	0.0677	0.0071	0.0095	0.0164	0.0211
15	0.0091	0.0167	0.0028	0.0126	0.0099	0.0177	0.0037	0.0045	0.0096	0.0058
16	0.0090	0.0077	0.0031	0.0119	0.0228	0.0099	0.0063	0.0110	0.0102	0.0058
17	0.0076	0.0089	0.0018	0.0092	0.0045	0.0090	0.0067	0.0073	0.0069	0.0026
18	0.0074	0.0091	0.0018	0.0018	0.0188	0.0047	0.0091	0.0064	0.0074	0.0054
19	0.0052	0.0128	0.0011	0.0068	0.0818	0.0105	0.0070	0.0025	0.0160	0.0269
20	0.0058	0.0173	0.0013	0.0017	0.0209	0.0074	0.0029	0.0021	0.0074	0.0076

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TABLE 28 Distribution of Radioactivity (% Applied Dose) at 24 h Post Dose Following Topical Application of [^{14}C]-Isopyrazam Spray Dilution 2 (Test Preparation 6, 0.31 g/L) to Human Split-Thickness Membranes

	Cell Number and Donor Number									
	Cell 77 0401	Cell 78 0401	Cell 79 0410	Cell 80 0410	Cell 81 0420	Cell 82 0420	Cell 83 0445	Cell 84 0445	Mean	SD
Skin Wash 6 h	62.54	49.63	71.92	73.66	39.68	49.52	60.01	47.20	56.77	12.22
Tissue Swab 6 h	14.10	30.53	20.28	13.87	48.48	42.85	17.04	39.51	28.34	13.89
Pipette Tip 6 h	0.12	0.03	0.04	0.04	0.04	0.05	0.06	0.02	0.05	0.03
Skin Wash 24 h	7.61	7.59	3.67	6.18	4.15	1.94	8.44	4.57	5.52	2.29
Tissue Swab 24 h	5.08	3.67	0.83	1.79	2.56	0.65	3.95	2.13	2.58	1.55
Pipette Tip 24 h	0.01	0.01	0.00	0.01	0.00	0.01	0.00	0.00	0.01	0.00
Donor Chamber Wash	*0.04	*0.05	*0.02	0.17	*0.04	*0.05	0.39	*0.06	°0.10	°0.13
Stratum Corneum 1-2	0.33	0.36	0.17	0.24	0.81	0.29	0.33	0.30	0.35	0.19
Stratum Corneum 3-5	0.40	0.26	0.23	0.25	0.69	0.35	0.59	0.60	0.42	0.18
Stratum Corneum 6-10	0.63	0.46	0.27	0.26	0.73	0.30	0.74	0.51	0.49	0.20
Stratum Corneum 11-15	0.56	0.39	0.17	0.29	0.37	0.14	0.59	0.29	0.35	0.16
Stratum Corneum 16-20	0.45	0.38	0.17	0.17	0.22	0.11	0.33	0.17	0.25	0.12
Unexposed Skin	0.04	0.03	0.01	0.04	0.01	0.04	0.49	0.03	0.08	0.16
Exposed Skin	4.41	3.29	0.74	0.98	0.54	0.52	2.23	1.11	1.73	1.45
Receptor Fluid	3.40	2.51	1.34	1.86	1.13	2.15	3.29	2.32	2.25	0.82
Receptor Chamber Wash	0.09	*0.06	*0.03	0.14	*0.05	*0.05	0.10	*0.05	°0.07	°0.04
Mass Balance	99.80	99.26	99.89	99.94	99.51	99.00	98.59	98.87	99.36	0.51

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TABLE 29 Cumulative Absorption (% Applied Dose) of [^{14}C]-Isopyrazam into Receptor Fluid Following Topical Application of [^{14}C]-Isopyrazam Spray Dilution 2 (Test Preparation 6, 0.31 g/L) to Human Split-Thickness Membranes

	Cell Number and Donor Number									
Time (h)	Cell 77 0401	Cell 78 0401	Cell 79 0410	Cell 80 0410	Cell 81 0420	Cell 82 0420	Cell 83 0445	Cell 84 0445	Mean	SD
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2	0.45	0.45	0.47	0.52	*0.05	0.24	0.32	0.57	°0.38	°0.17
4	0.84	0.68	0.60	0.74	0.13	0.43	0.86	0.80	0.63	0.25
6	1.20	0.97	0.86	0.92	0.22	0.67	1.22	0.83	0.86	0.32
8	1.73	1.37	1.01	1.25	0.48	1.21	1.73	1.56	1.29	0.41
12	2.23	1.96	1.13	1.45	0.77	1.52	2.31	2.04	1.68	0.55
24	3.40	2.51	1.34	1.86	1.13	2.15	3.29	2.32	2.25	0.82

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TABLE 30 Distribution of Radioactivity (µg equiv./cm^2) at 24 h Post Dose Following Topical Application of [^{14}C]-Isopyrazam Spray Dilution 2 (Test Preparation 6, 0.31 g/L) to Human Split-Thickness Membranes

	Cell Number and Donor Number									
	Cell 77 0401	Cell 78 0401	Cell 79 0410	Cell 80 0410	Cell 81 0420	Cell 82 0420	Cell 83 0445	Cell 84 0445	Mean	SD
Skin Wash 6 h	2.055	1.631	2.363	2.420	1.304	1.627	1.972	1.551	1.865	0.402
Tissue Swab 6 h	0.463	1.003	0.666	0.456	1.593	1.408	0.560	1.298	0.931	0.456
Pipette Tip 6 h	0.004	0.001	0.001	0.001	0.001	0.002	0.002	0.001	0.002	0.001
Skin Wash 24 h	0.250	0.249	0.121	0.203	0.136	0.064	0.277	0.150	0.181	0.075
Tissue Swab 24 h	0.167	0.121	0.027	0.059	0.084	0.021	0.130	0.070	0.085	0.051
Pipette Tip 24 h	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Donor Chamber Wash	*0.001	*0.002	*0.000	0.006	*0.001	*0.002	0.013	*0.002	°0.003	°0.004
Stratum Corneum 1-2	0.011	0.012	0.005	0.008	0.026	0.009	0.011	0.010	0.012	0.006
Stratum Corneum 3-5	0.013	0.008	0.008	0.008	0.023	0.011	0.019	0.020	0.014	0.006
Stratum Corneum 6-10	0.021	0.015	0.009	0.009	0.024	0.010	0.024	0.017	0.016	0.007
Stratum Corneum 11-15	0.018	0.013	0.005	0.010	0.012	0.005	0.019	0.009	0.011	0.005
Stratum Corneum 16-20	0.015	0.013	0.005	0.005	0.007	0.003	0.011	0.006	0.008	0.004
Unexposed Skin	0.001	0.001	0.000	0.001	0.000	0.001	0.016	0.001	0.003	0.005
Exposed Skin	0.145	0.108	0.024	0.032	0.018	0.017	0.073	0.037	0.057	0.048
Receptor Fluid	0.112	0.083	0.044	0.061	0.037	0.071	0.108	0.076	0.074	0.027
Receptor Chamber Wash	0.003	*0.002	*0.001	0.005	*0.002	*0.002	0.003	*0.002	°0.002	°0.001
Mass Balance	3.279	3.262	3.282	3.284	3.270	3.253	3.240	3.249	3.265	0.017

*=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

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TABLE 31 Cumulative Absorption (µg equiv./cm^2) of [^{14}C]-Isopyrazam into Receptor Fluid Following Topical Application of [^{14}C]-Isopyrazam Spray Dilution 2 (Test Preparation 6, 0.31 g/L) to Human Split-Thickness Membranes

	Cell Number and Donor Number									
	Cell 77	Cell 78	Cell 79	Cell 80	Cell 81	Cell 82	Cell 83	Cell 84		
Time (h)	0401	0401	0410	0410	0420	0420	0445	0445	Mean	SD
0	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
2	0.015	0.015	0.015	0.017	*0.002	0.008	0.011	0.019	°0.013	°0.006
4	0.028	0.022	0.020	0.024	0.004	0.014	0.028	0.026	0.021	0.008
6	0.039	0.032	0.028	0.030	0.007	0.022	0.040	0.027	0.028	0.010
8	0.057	0.045	0.033	0.041	0.016	0.040	0.057	0.051	0.042	0.014
12	0.073	0.065	0.037	0.048	0.025	0.050	0.076	0.067	0.055	0.018
24	0.112	0.083	0.044	0.061	0.037	0.071	0.108	0.076	0.074	0.027

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TABLE 32 Distribution of Radioactivity (µg equiv./cm^2) in the Stratum Corneum at 24 h Post Dose Following Topical Application of [^{14}C]-Isopyrazam Spray Dilution 2 (Test Preparation 6, 0.31 g/L) to Human Split-Thickness Membranes

	Distribution of Radioactivity at 24 h									
Tape Strip No.	Cell 77 0401	Cell 78 0401	Cell 79 0410	Cell 80 0410	Cell 81 0420	Cell 82 0420	Cell 83 0445	Cell 84 0445	Mean	SD
1	0.0057	0.0035	0.0022	0.0036	0.0143	0.0047	0.0044	0.0042	0.0054	0.0038
2	0.0052	0.0081	0.0033	0.0042	0.0121	0.0047	0.0064	0.0055	0.0062	0.0028
3	0.0034	0.0011	0.0025	0.0021	0.0096	0.0052	0.0072	0.0052	0.0045	0.0028
4	0.0045	0.0037	0.0028	0.0032	0.0076	0.0033	0.0063	0.0096	0.0051	0.0025
5	0.0051	0.0037	0.0022	0.0030	0.0055	0.0029	0.0059	0.0049	0.0041	0.0014
6	0.0063	0.0066	0.0025	0.0022	0.0032	0.0018	0.0043	0.0023	0.0037	0.0019
7	0.0055	0.0032	0.0015	0.0016	0.0049	0.0043	0.0053	0.0086	0.0044	0.0023
8	0.0034	0.0022	0.0025	0.0016	0.0045	0.0018	0.0055	0.0025	0.0030	0.0014
9	0.0028	0.0016	0.0013	0.0021	0.0050	0.0012	0.0066	0.0015	0.0028	0.0020
10	0.0027	0.0016	0.0011	0.0011	0.0063	0.0007	0.0025	0.0019	0.0022	0.0018
11	0.0061	0.0026	0.0014	0.0049	0.0032	0.0012	0.0061	0.0023	0.0035	0.0020
12	0.0053	0.0017	0.0007	0.0020	0.0015	0.0011	0.0045	0.0010	0.0022	0.0017
13	0.0033	0.0018	0.0018	0.0011	0.0024	0.0009	0.0036	0.0018	0.0021	0.0010
14	0.0020	0.0023	0.0010	0.0012	0.0030	0.0007	0.0024	0.0029	0.0019	0.0009
15	0.0015	0.0046	0.0006	0.0003	0.0021	0.0007	0.0028	0.0014	0.0018	0.0014
16	0.0030	0.0019	0.0016	0.0014	0.0004	0.0004	0.0013	0.0014	0.0014	0.0008
17	0.0032	0.0045	0.0025	0.0014	0.0021	0.0005	0.0021	0.0013	0.0022	0.0012
18	0.0032	0.0024	0.0007	0.0012	0.0023	0.0007	0.0036	0.0009	0.0019	0.0011
19	0.0022	0.0017	0.0003	0.0004	0.0016	0.0013	0.0020	0.0008	0.0013	0.0007
20	0.0031	0.0021	0.0003	0.0011	0.0009	0.0006	0.0018	0.0011	0.0014	0.0009

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FIGURES SECTION

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FIGURE 1 Individual Absorption Profiles for [^{14}C]-Cyproconazole (% Applied Dose) in Receptor Fluid Following Topical Application of [^{14}C]-Cyproconazole Formulation Concentrate (Test Preparation 1, 80 g/L) to Human Split-Thickness Membranes

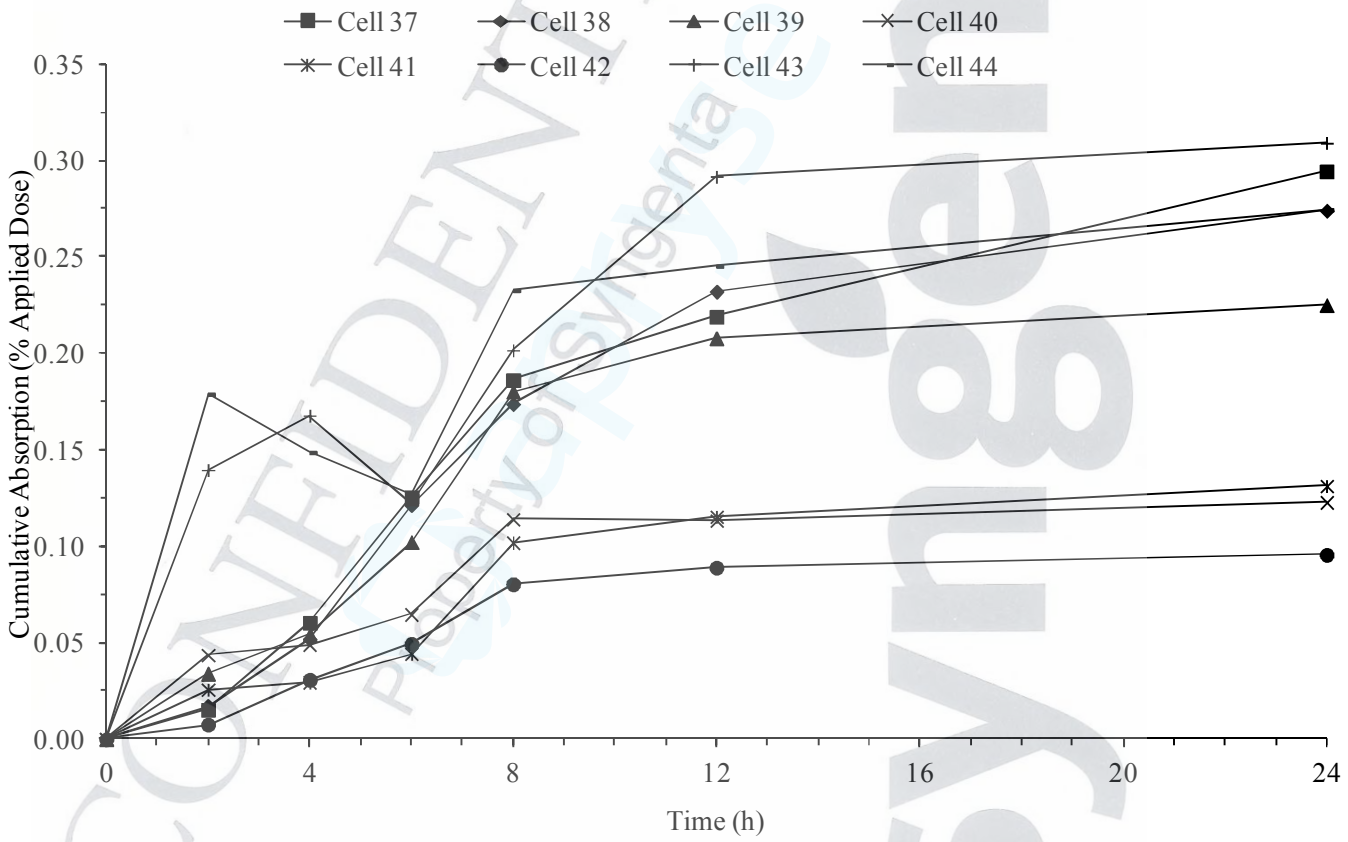

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FIGURE 2 **Absorption Profile for [^{14}C]-Cyproconazole (% Applied Dose) in Receptor Fluid Following Topical Application of [^{14}C]-Cyproconazole Formulation Concentrate (Test Preparation 1, 80 g/L) to Human Split-Thickness Membranes (Mean + SD, n = 8)**

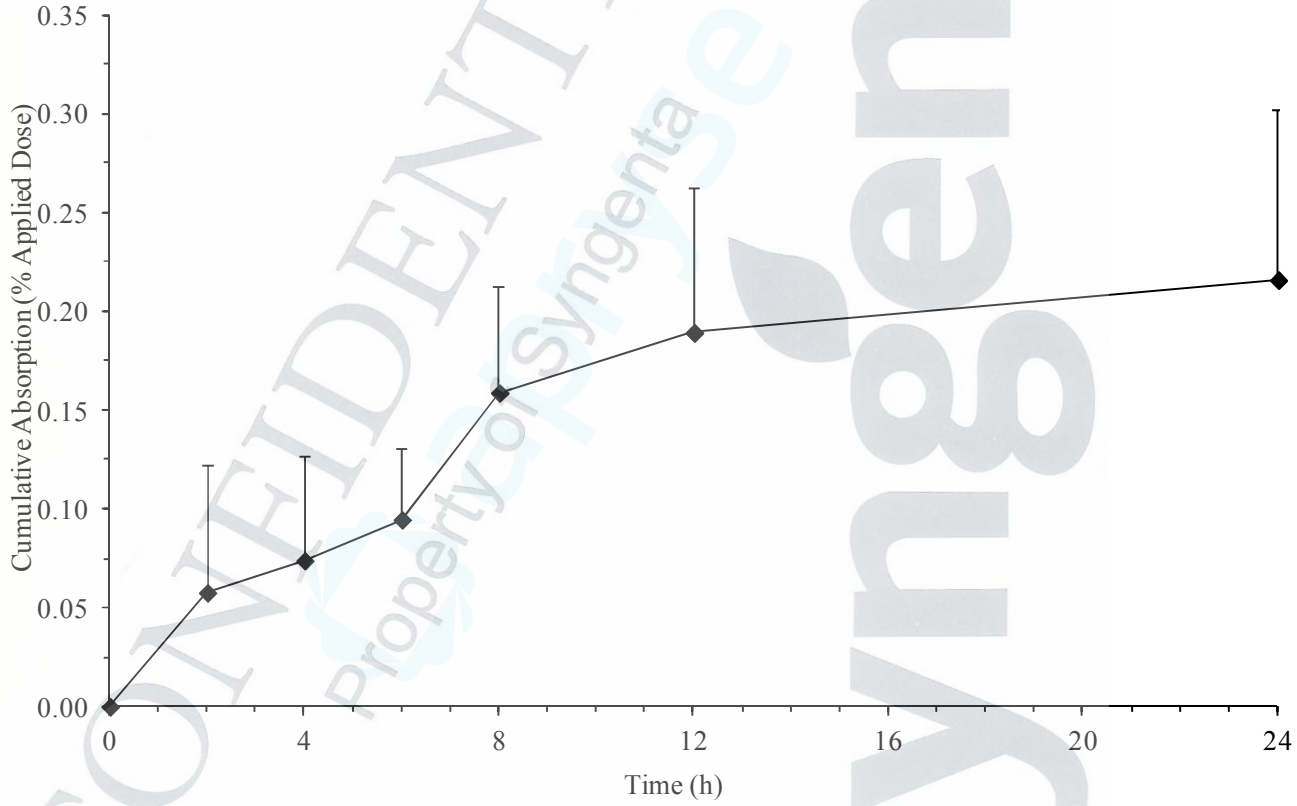

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FIGURE 3 **Absorption Profile of [^{14}C]-Cyproconazole (µg equiv./cm^2) in Receptor Fluid Following Topical Application of [^{14}C]-Cyproconazole Formulation Concentrate (Test Preparation 1, 80 g/L) to Human Split-Thickness Membranes (Mean + SD, n = 8)**

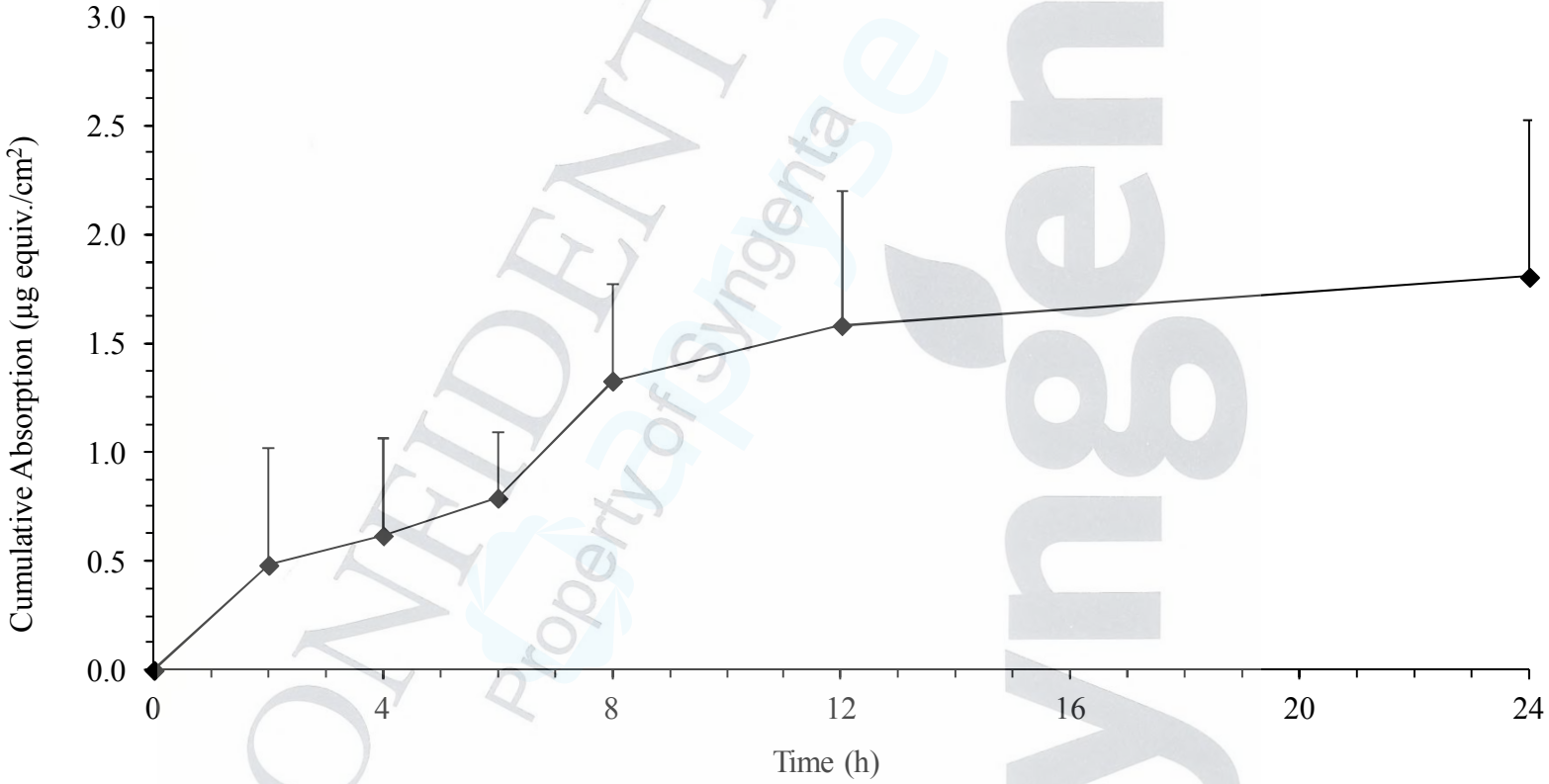

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FIGURE 4 Distribution of [^{14}C]-Cyproconazole (µg equiv./cm^2) in the Stratum Corneum at 24 h Post Dose Following Topical Application of [^{14}C]-Cyproconazole Formulation Concentrate (Test Preparation 1, 80 g/L) to Human Split-Thickness Membranes (Mean + SD, n = 8)

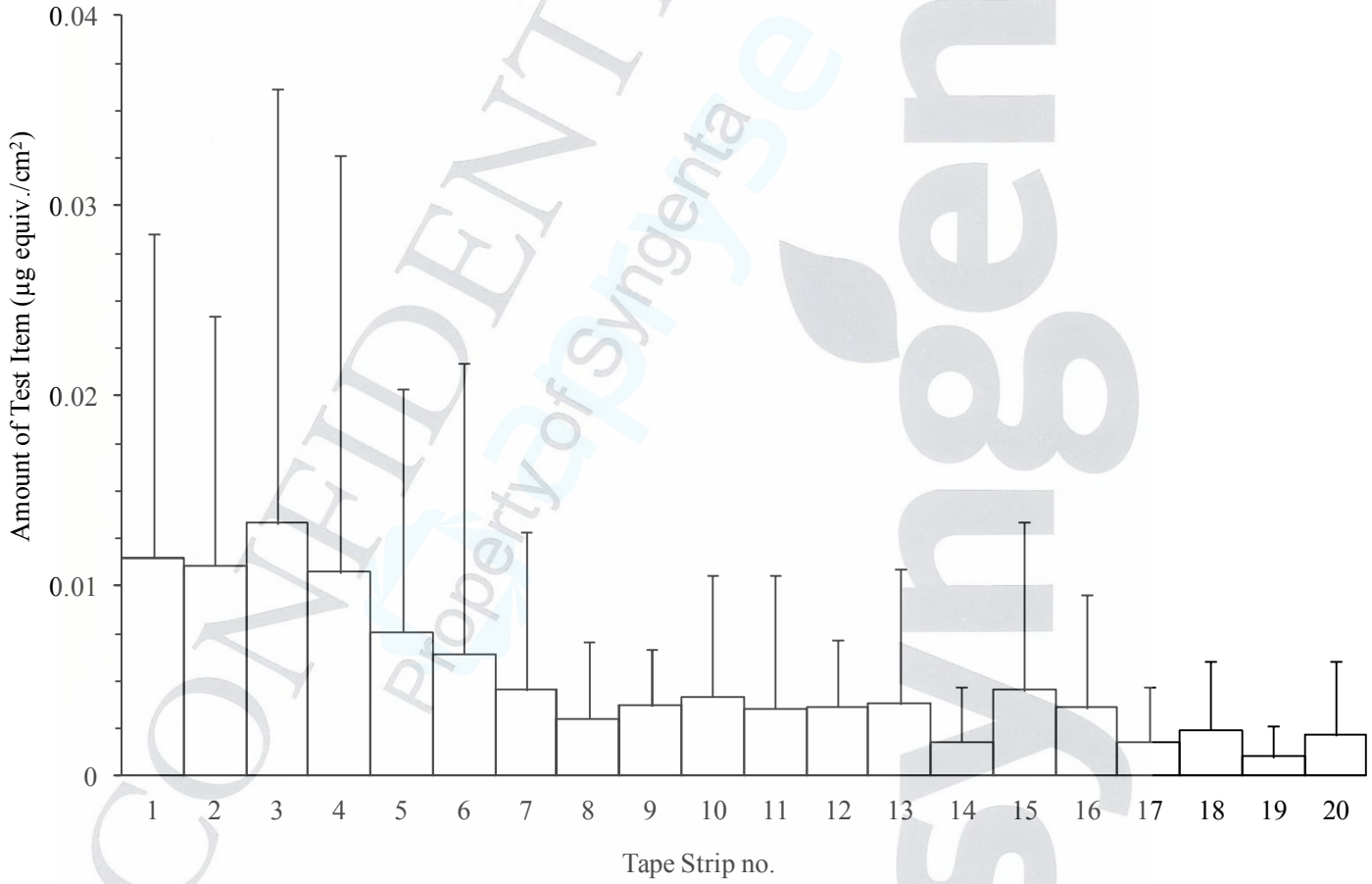

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FIGURE 5 Individual Absorption Profiles for [^{14}C]-Cyproconazole (% Applied Dose) in Receptor Fluid Following Topical Application of [^{14}C]-Cyproconazole Spray Dilution 1 (Test Preparation 2, 0.8 g/L) to Human Split-Thickness Membranes

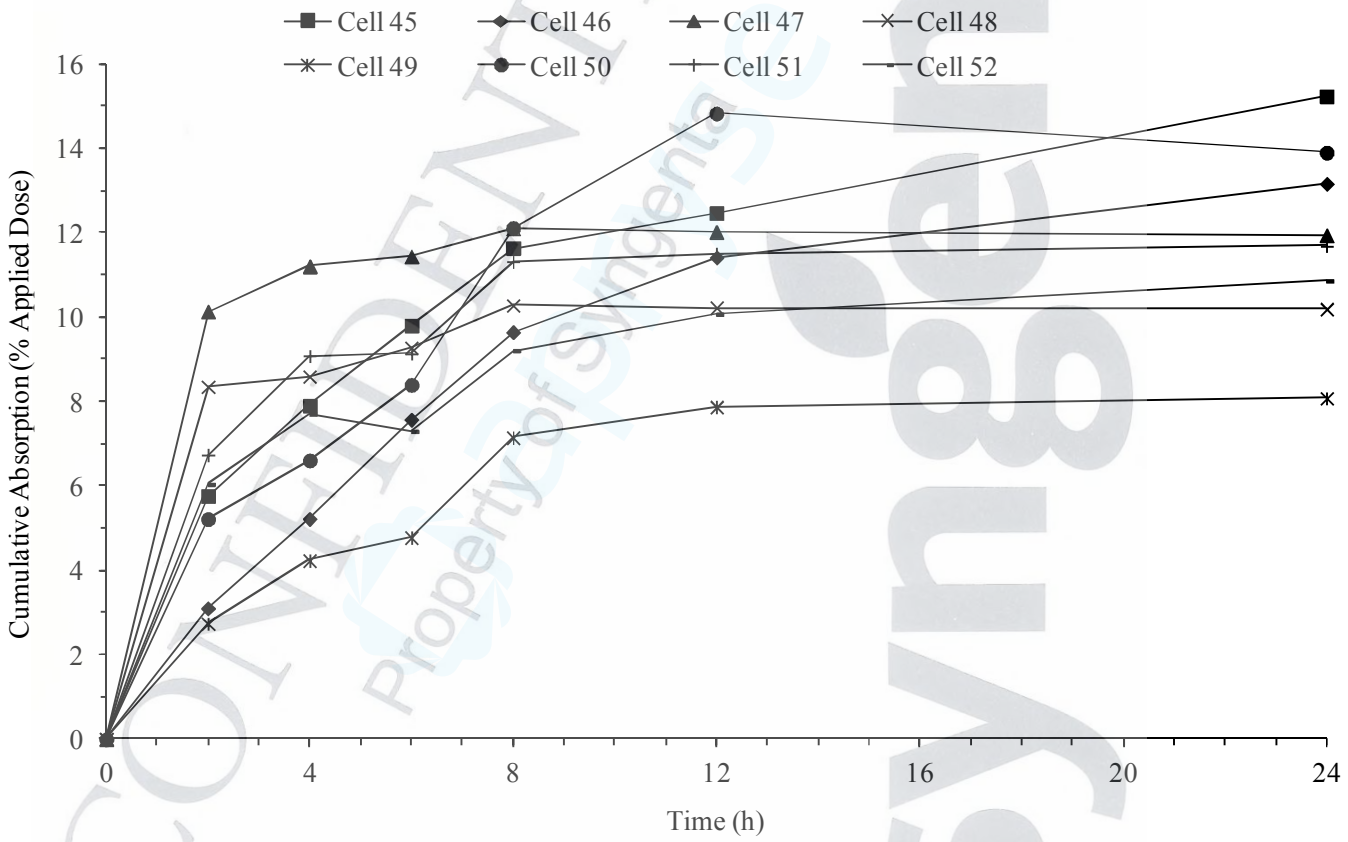

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FIGURE 6 Absorption Profile for [^{14}C]-Cyproconazole (% Applied Dose) in Receptor Fluid Following Topical Application of [^{14}C]-Cyproconazole Spray Dilution 1 (Test Preparation 2, 0.8 g/L) to Human Split-Thickness Membranes (Mean + SD, n = 8)

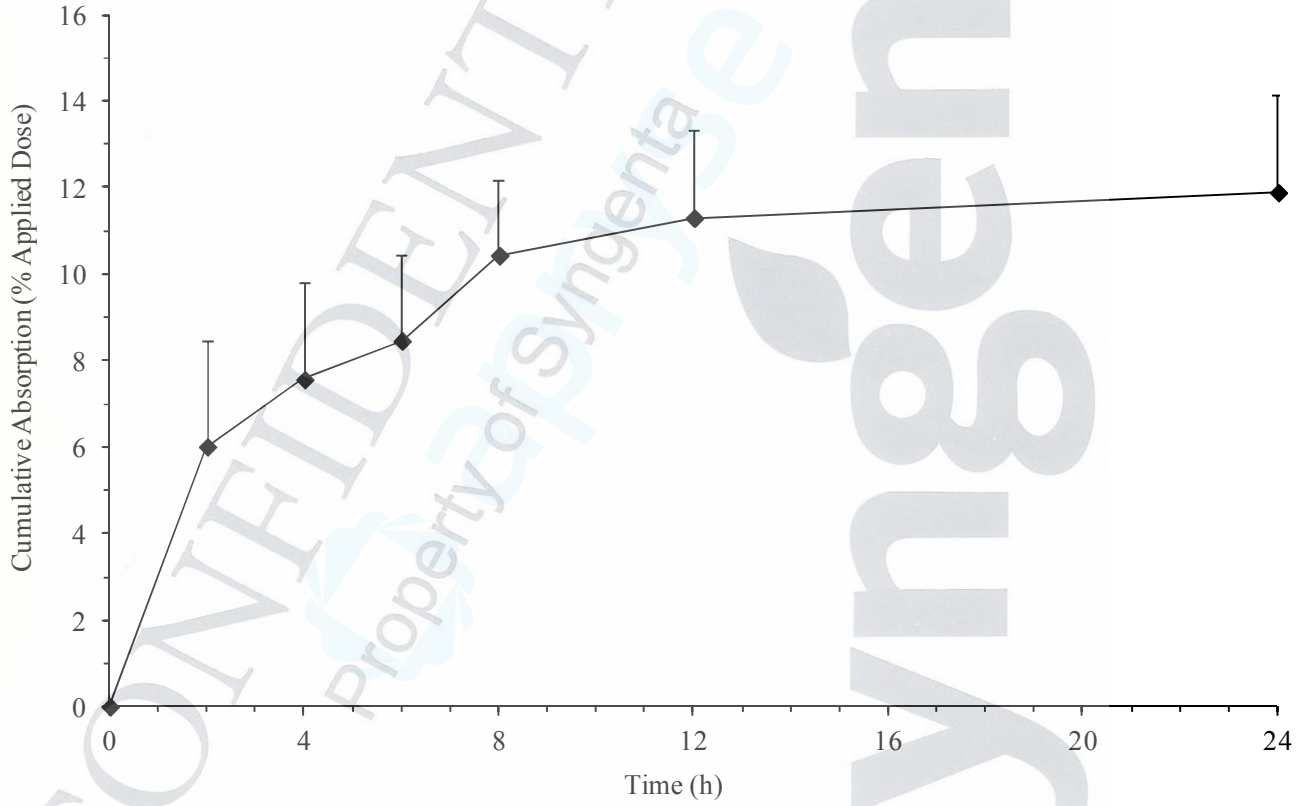

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FIGURE 7 Absorption Profile of [^{14}C]-Cyproconazole (µg equiv./cm^2) in Receptor Fluid Following Topical Application of [^{14}C]-Cyproconazole Spray Dilution 1 (Test Preparation 2, 0.8 g/L) to Human Split-Thickness Membranes (Mean + SD, n = 8)

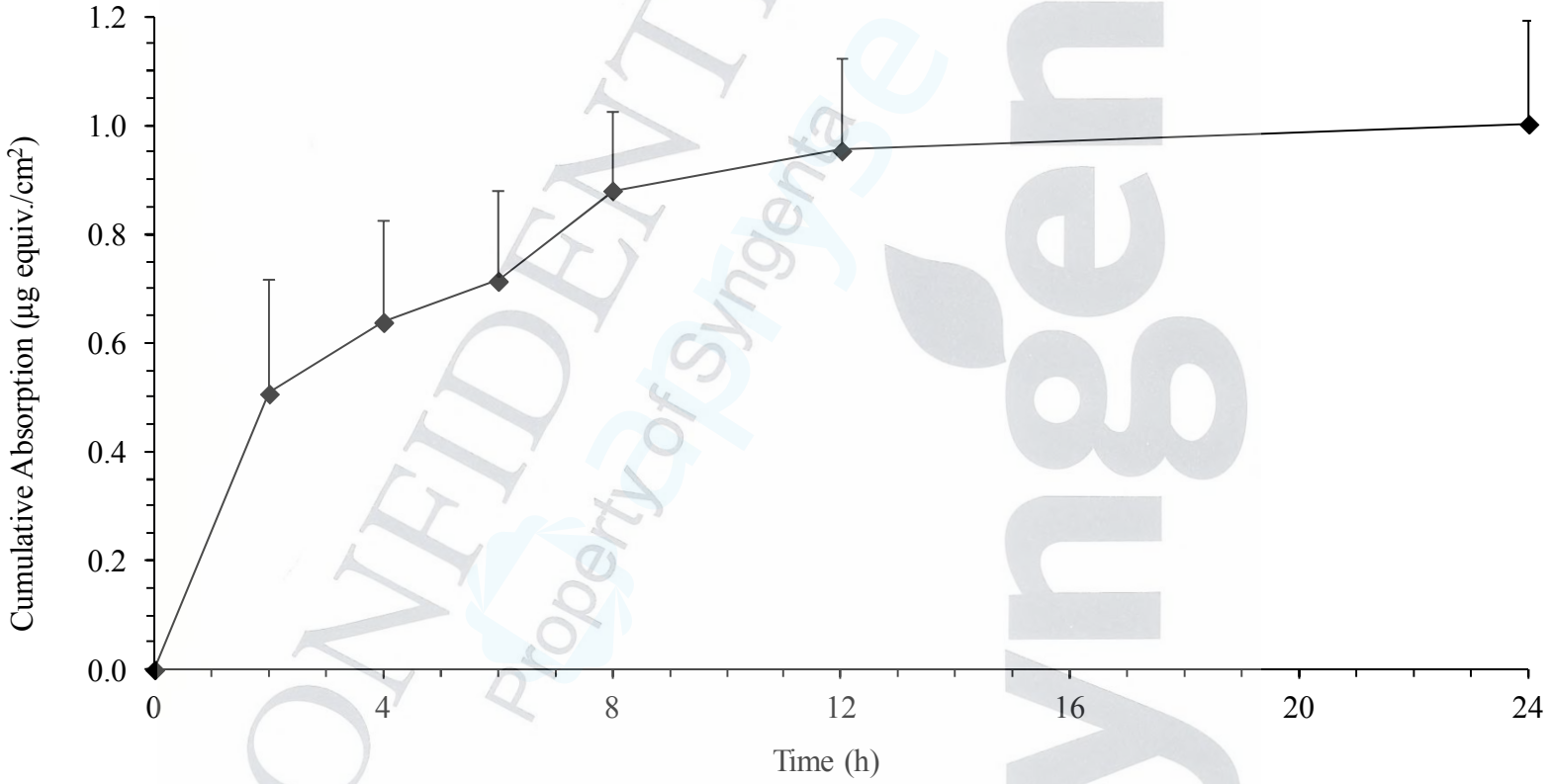

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FIGURE 8 **Distribution of [^{14}C]-Cyproconazole (µg equiv./cm^2) in the Stratum Corneum at 24 h Post Dose Following Topical Application of [^{14}C]-Cyproconazole Spray Dilution 1 (Test Preparation 2, 0.8 g/L) to Human Split-Thickness Membranes (Mean + SD, n = 8)**

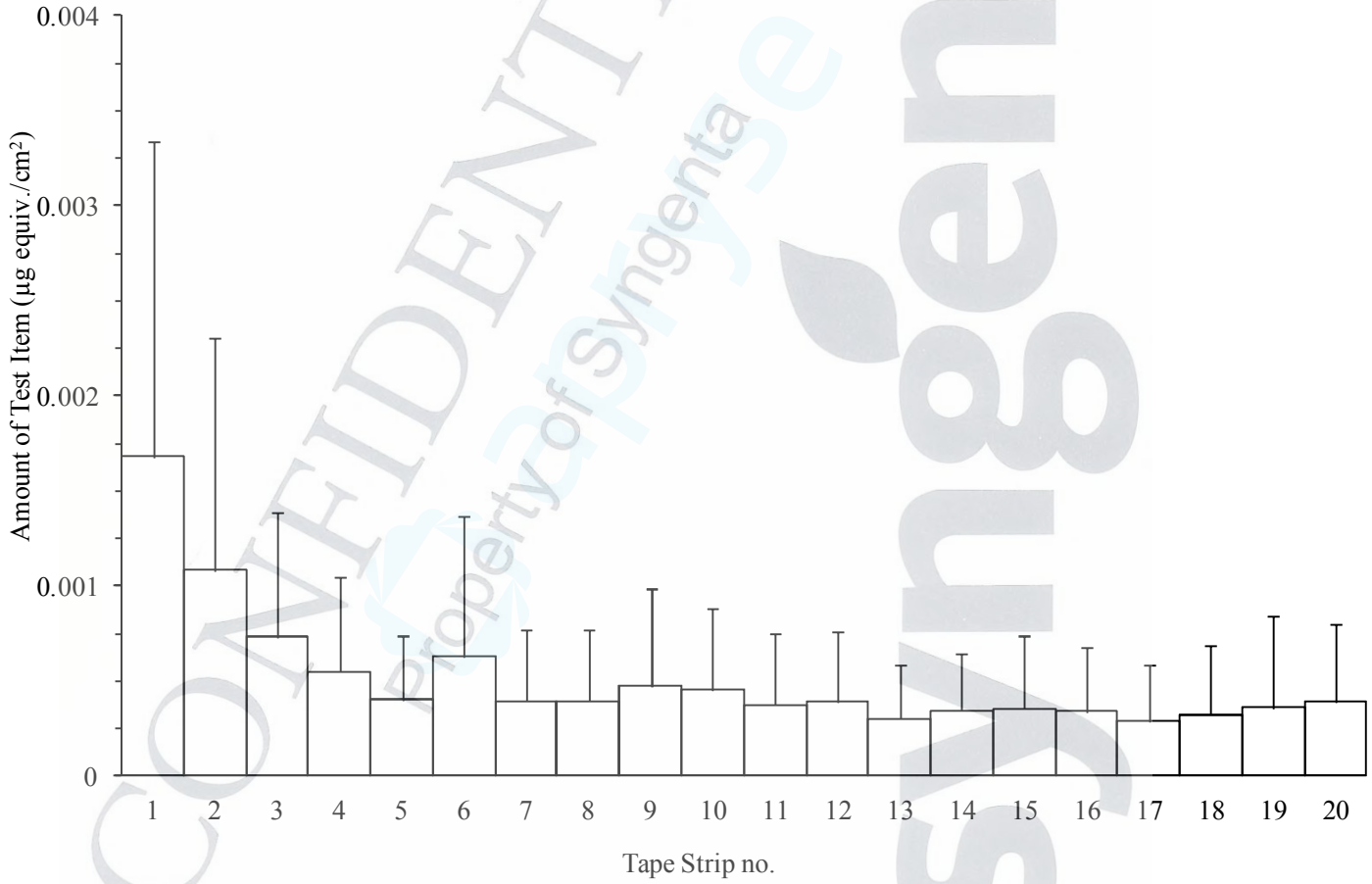

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FIGURE 9 Individual Absorption Profiles for [^{14}C]-Cyproconazole (% Applied Dose) in Receptor Fluid Following Topical Application of [^{14}C]-Cyproconazole Spray Dilution 2 (Test Preparation 3, 0.2 g/L) to Human Split-Thickness Membranes

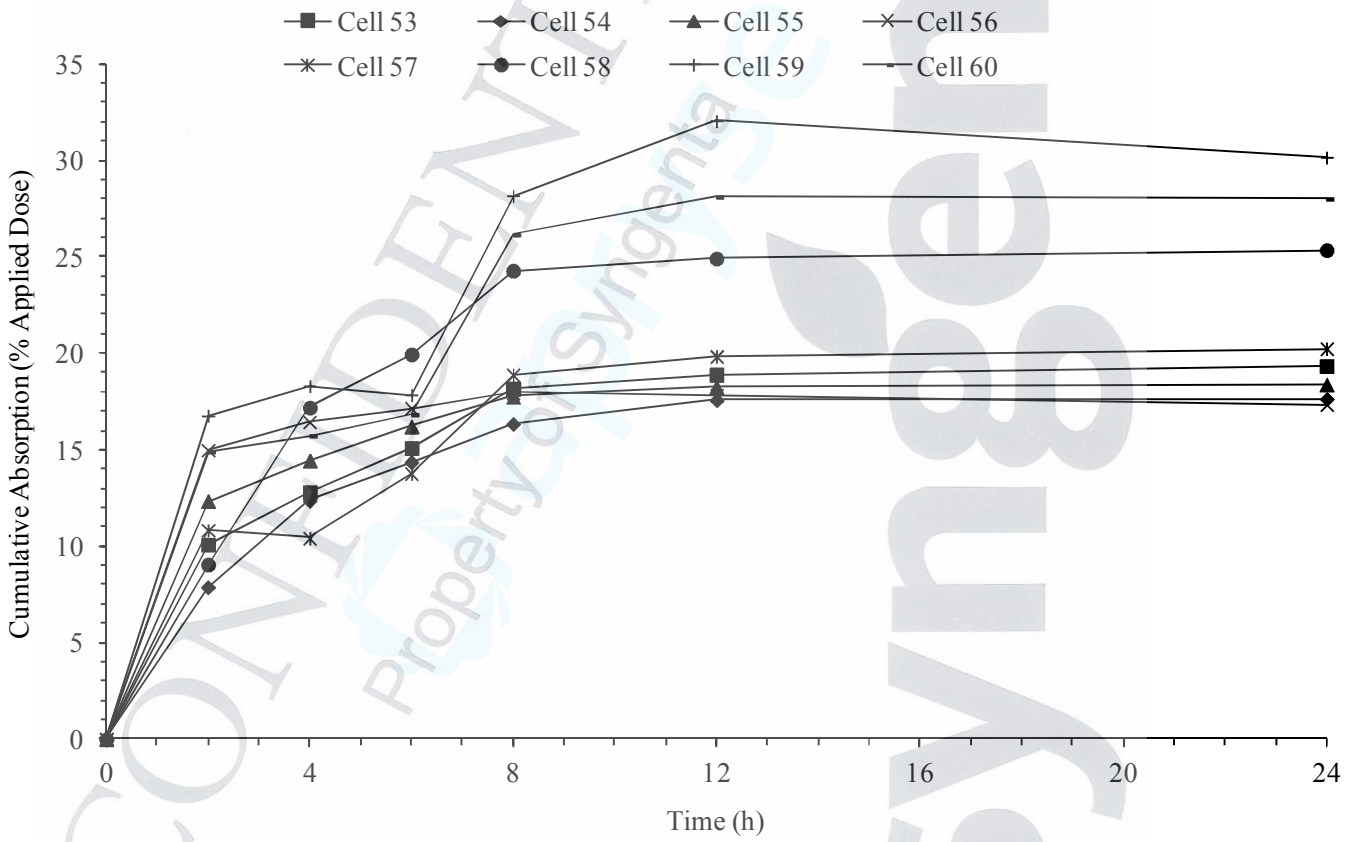

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FIGURE 10 Absorption Profile for [^{14}C]-Cyproconazole (% Applied Dose) in Receptor Fluid Following Topical Application of [^{14}C]-Cyproconazole Spray Dilution 2 (Test Preparation 3, 0.2 g/L) to Human Split-Thickness Membranes (Mean + SD, n = 8)

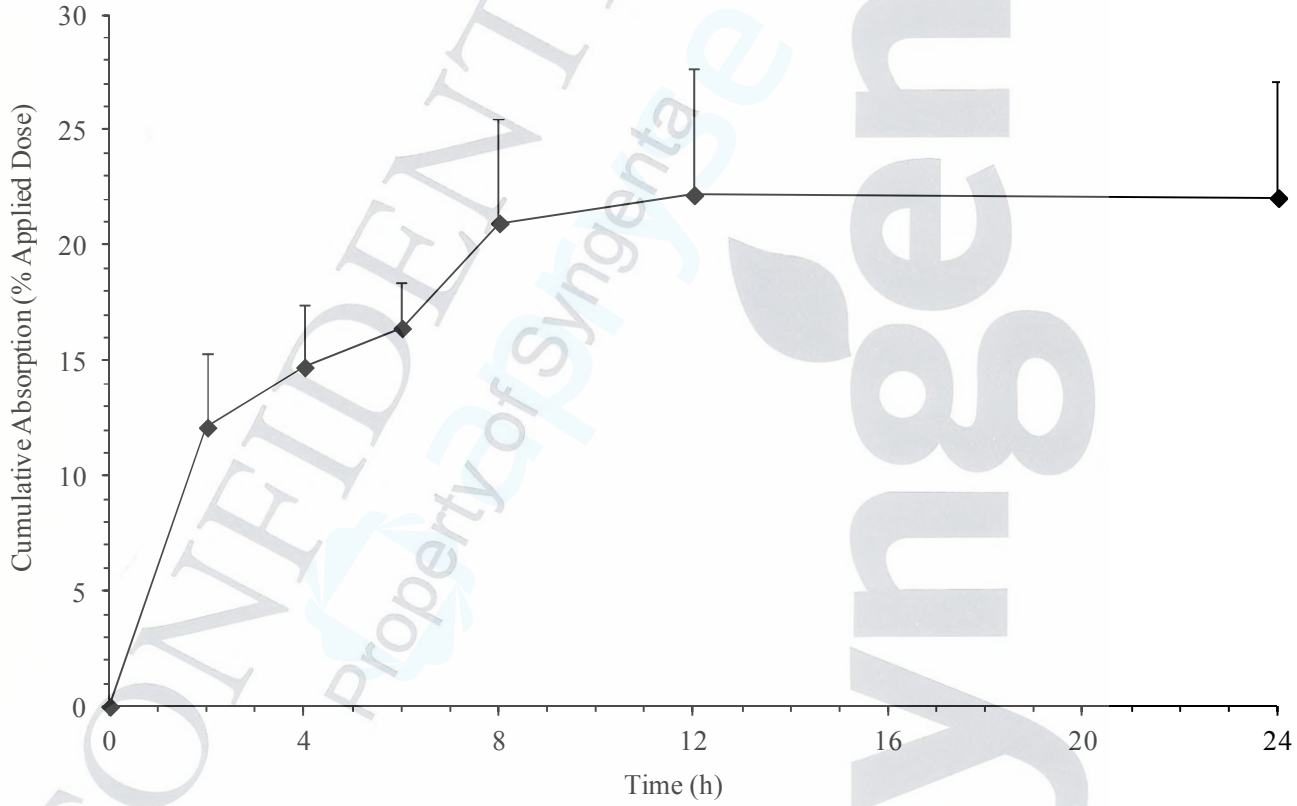

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FIGURE 11 Absorption Profile of [^{14}C]-Cyproconazole (µg equiv./cm^2) in Receptor Fluid Following Topical Application of [^{14}C]-Cyproconazole Spray Dilution 2 (Test Preparation 3, 0.2 g/L) to Human Split-Thickness Membranes (Mean + SD, n = 8)

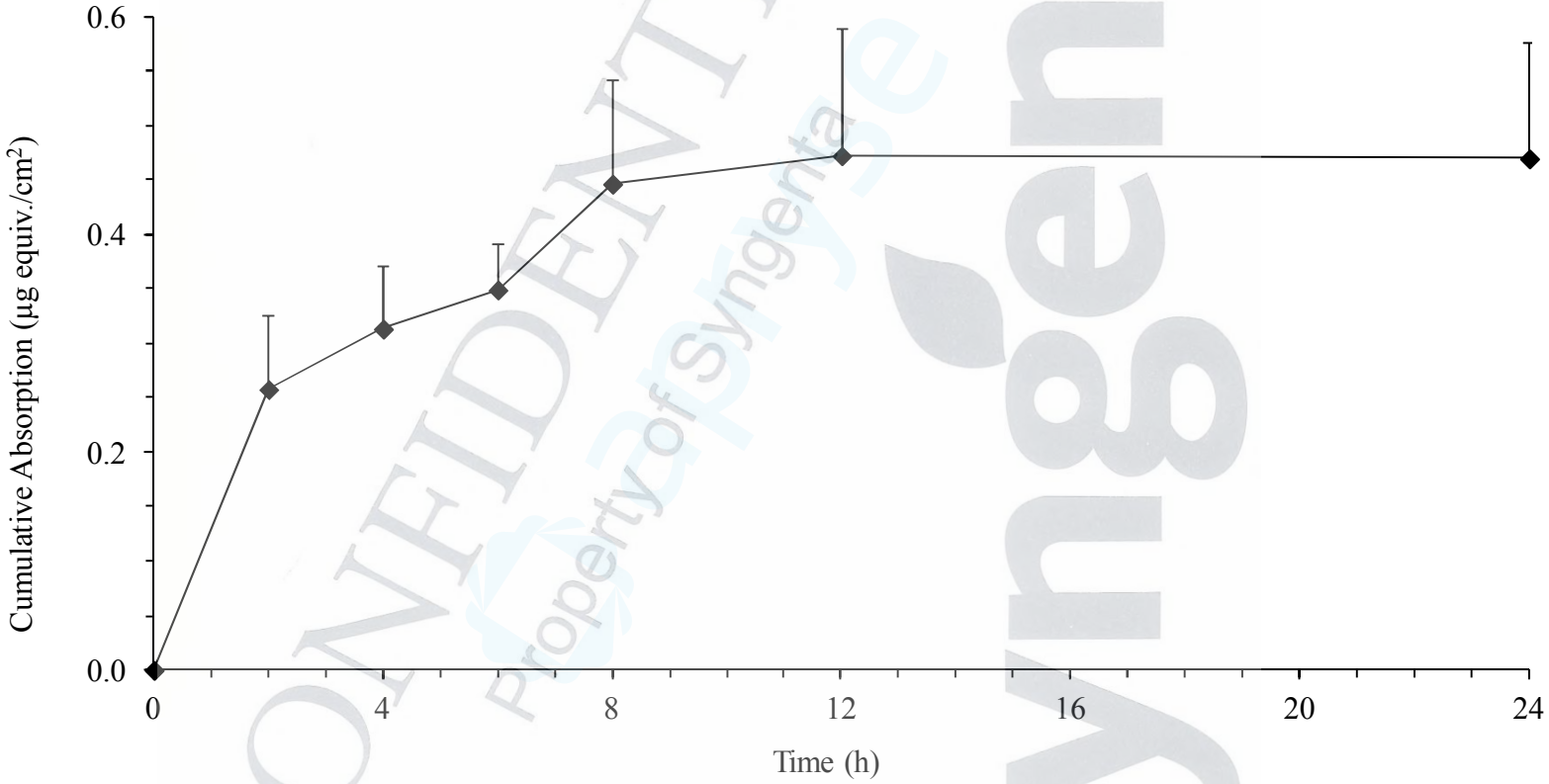

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FIGURE 12 **Distribution of [^{14}C]-Cyproconazole (µg equiv./cm^2) in the Stratum Corneum at 24 h Post Dose Following Topical Application of [^{14}C]-Cyproconazole Spray Dilution 2 (Test Preparation 3, 0.2 g/L) to Human Split-Thickness Membranes (Mean + SD, n = 8)**

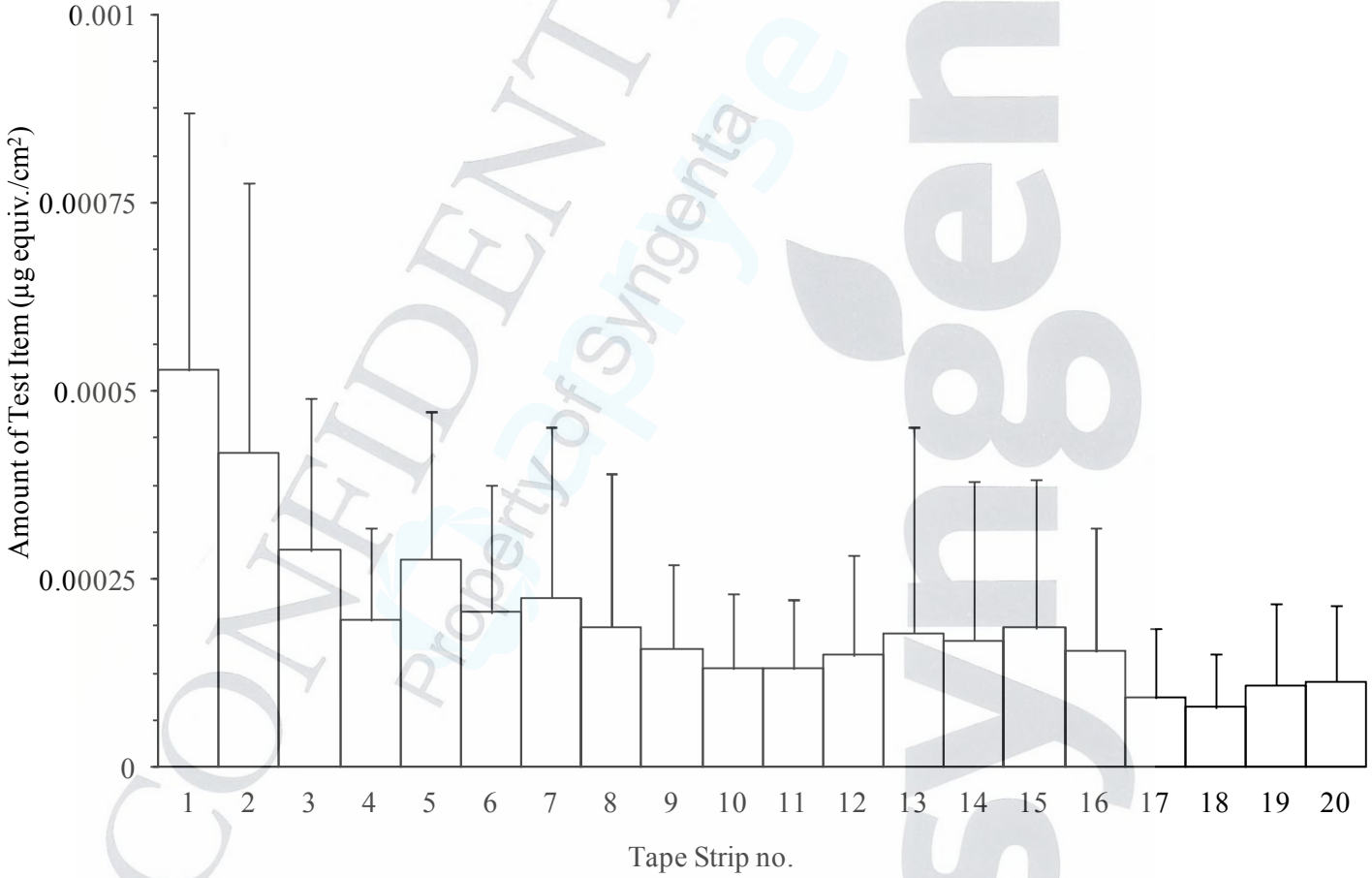

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FIGURE 13 **Individual Absorption Profiles for [^{14}C]-Isopyrazam (% Applied Dose) in Receptor Fluid Following Topical Application of [^{14}C]-Isopyrazam Formulation Concentrate (Test Preparation 4, 125 g/L) to Human Split-Thickness Membranes**

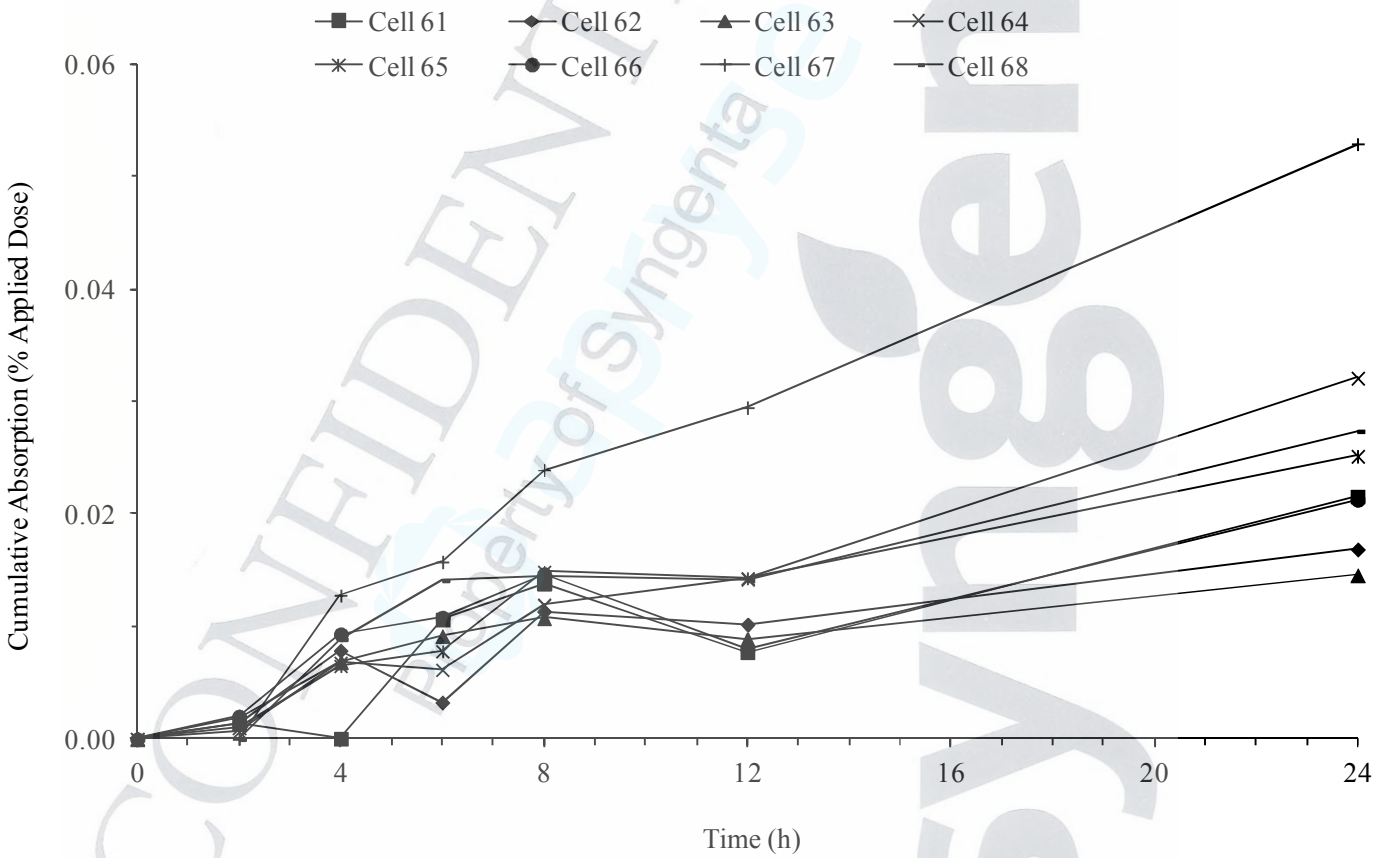

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FIGURE 14 Absorption Profile for [^{14}C]-Isopyrazam (% Applied Dose) in Receptor Fluid Following Topical Application of [^{14}C]-Isopyrazam Formulation Concentrate (Test Preparation 4, 125 g/L) to Human Split-Thickness Membranes (Mean + SD, n = 8)

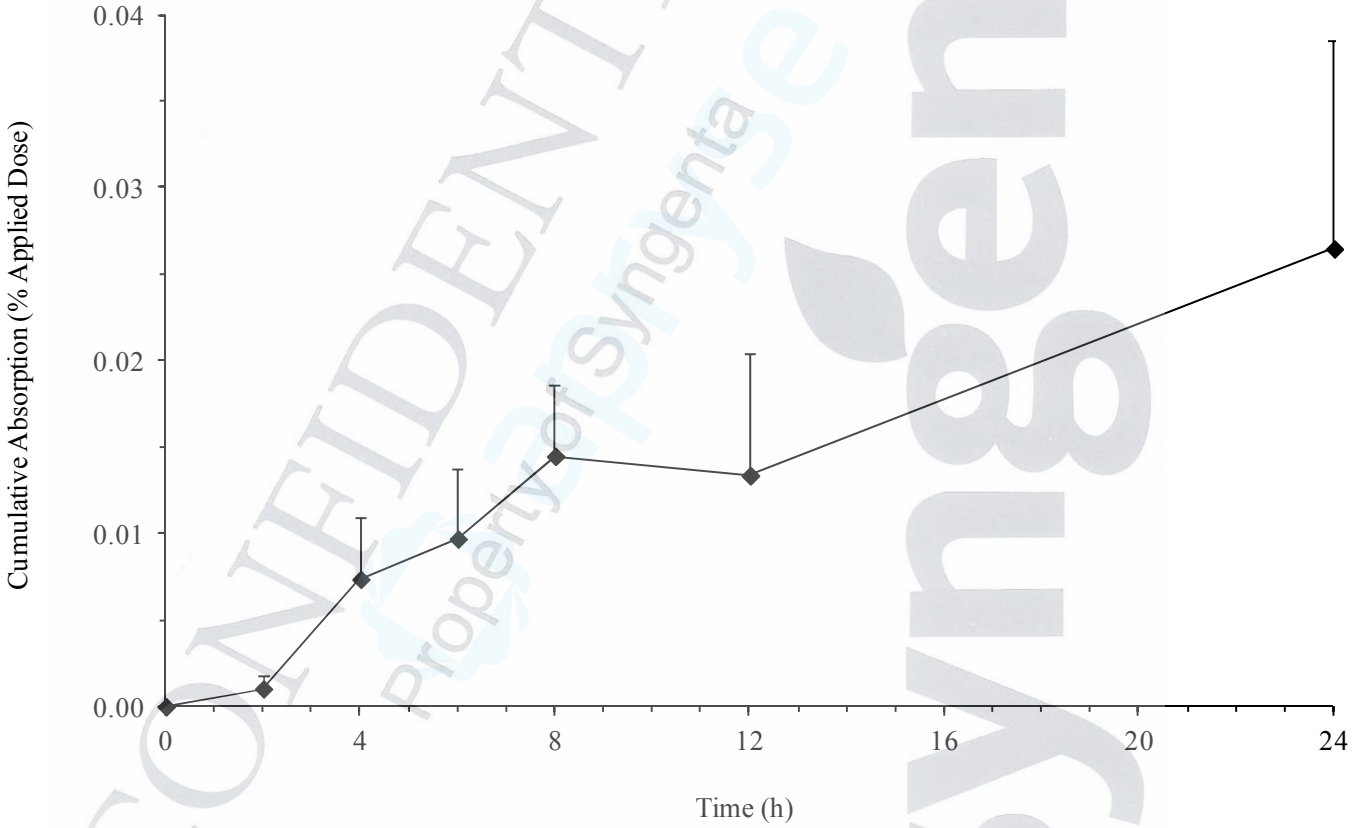

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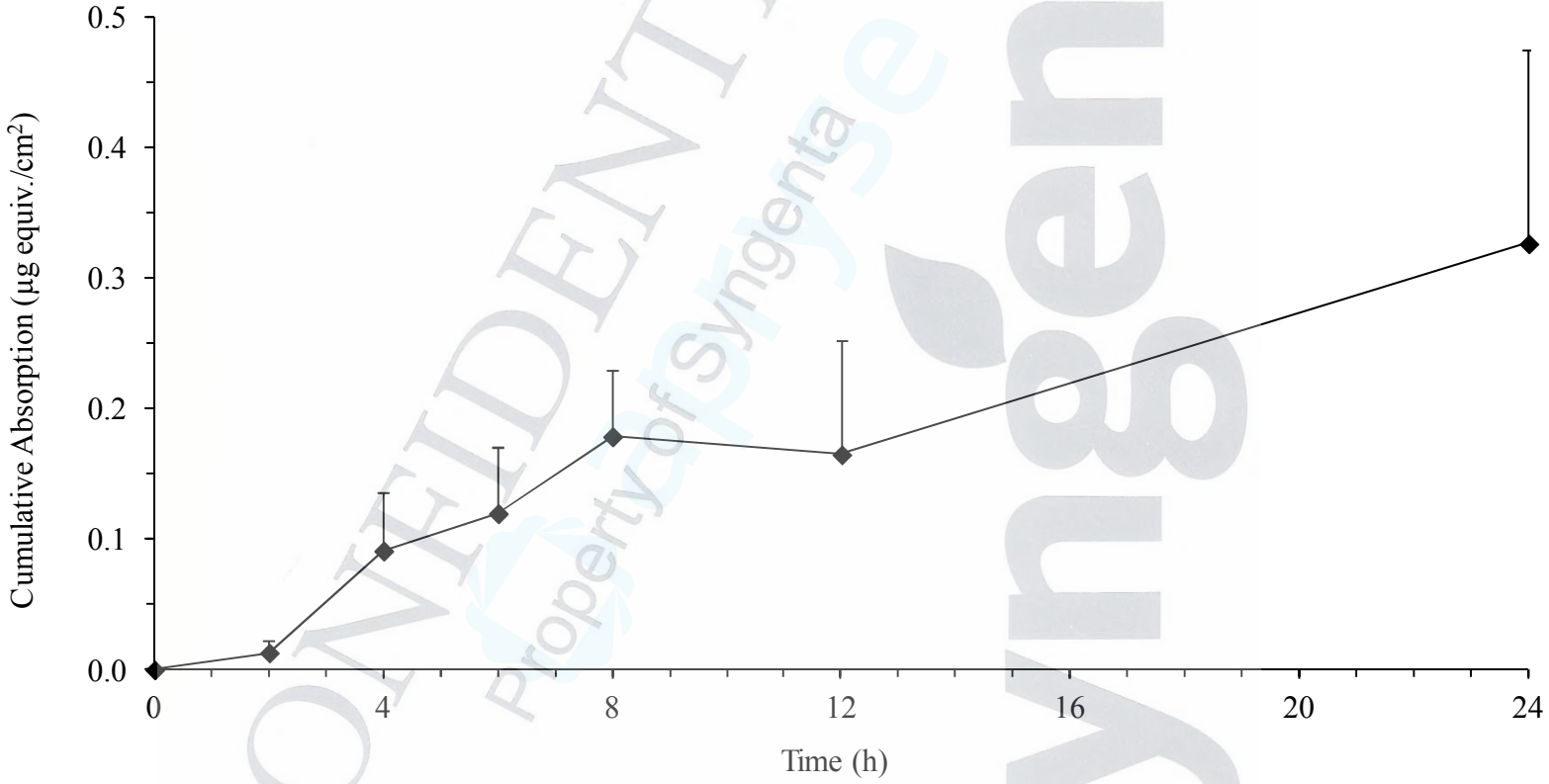
FIGURE 15 **Absorption Profile of [^{14}C]-Isopyrazam (µg equiv./cm^2) in Receptor Fluid Following Topical Application of [^{14}C]-Isopyrazam Formulation Concentrate (Test Preparation 4, 125 g/L) to Human Split-Thickness Membranes (Mean + SD, n = 8)**



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Mod. 005C

FIGURE 16 Distribution of [^{14}C]-Isopyrazam (µg equiv./cm^2) in the Stratum Corneum at 24 h Post Dose Following Topical Application of [^{14}C]-Isopyrazam Formulation Concentrate (Test Preparation 4, 125 g/L) to Human Split-Thickness Membranes (Mean + SD, n = 8)

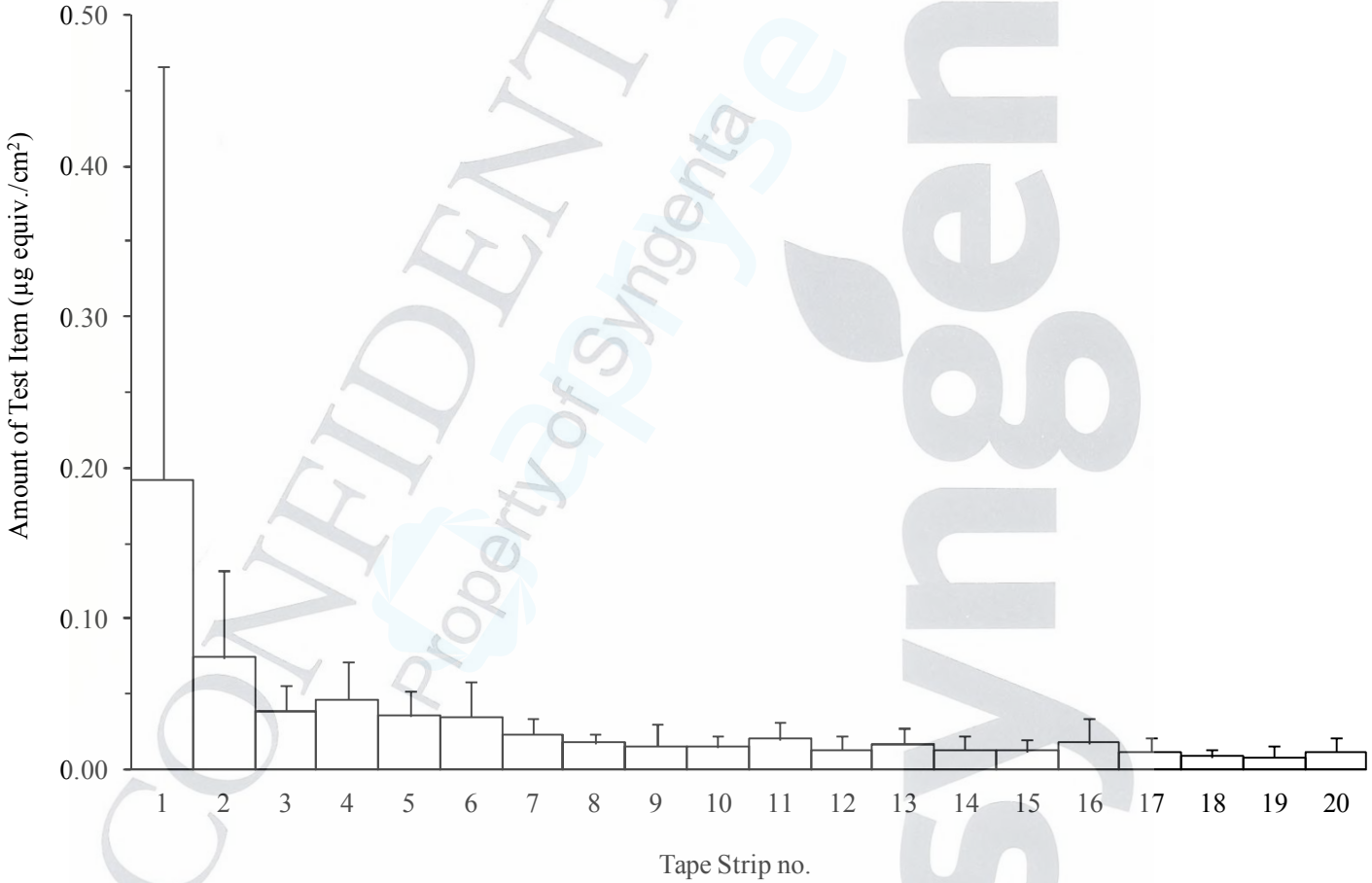

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FIGURE 17 Individual Absorption Profiles for [^{14}C]-Isopyrazam (% Applied Dose) in Receptor Fluid Following Topical Application of [^{14}C]-Isopyrazam Spray Dilution 1 (Test Preparation 5, 1.25 g/L) to Human Split-Thickness Membranes

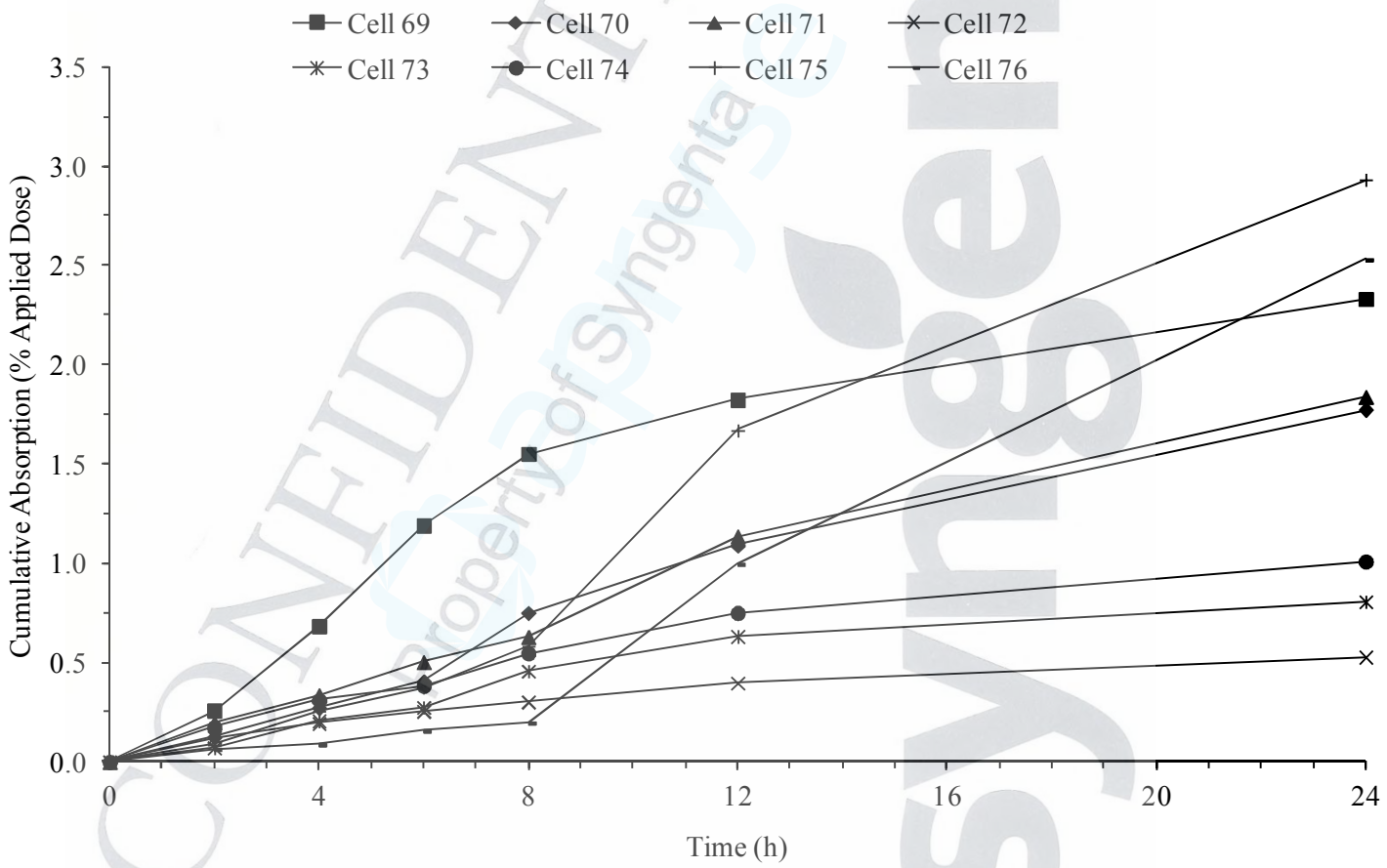

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FIGURE 18 Absorption Profile for [^{14}C]-Isopyrazam (% Applied Dose) in Receptor Fluid Following Topical Application of [^{14}C]-Isopyrazam Spray Dilution 1 (Test Preparation 5, 1.25 g/L) to Human Split-Thickness Membranes (Mean + SD, n = 8)

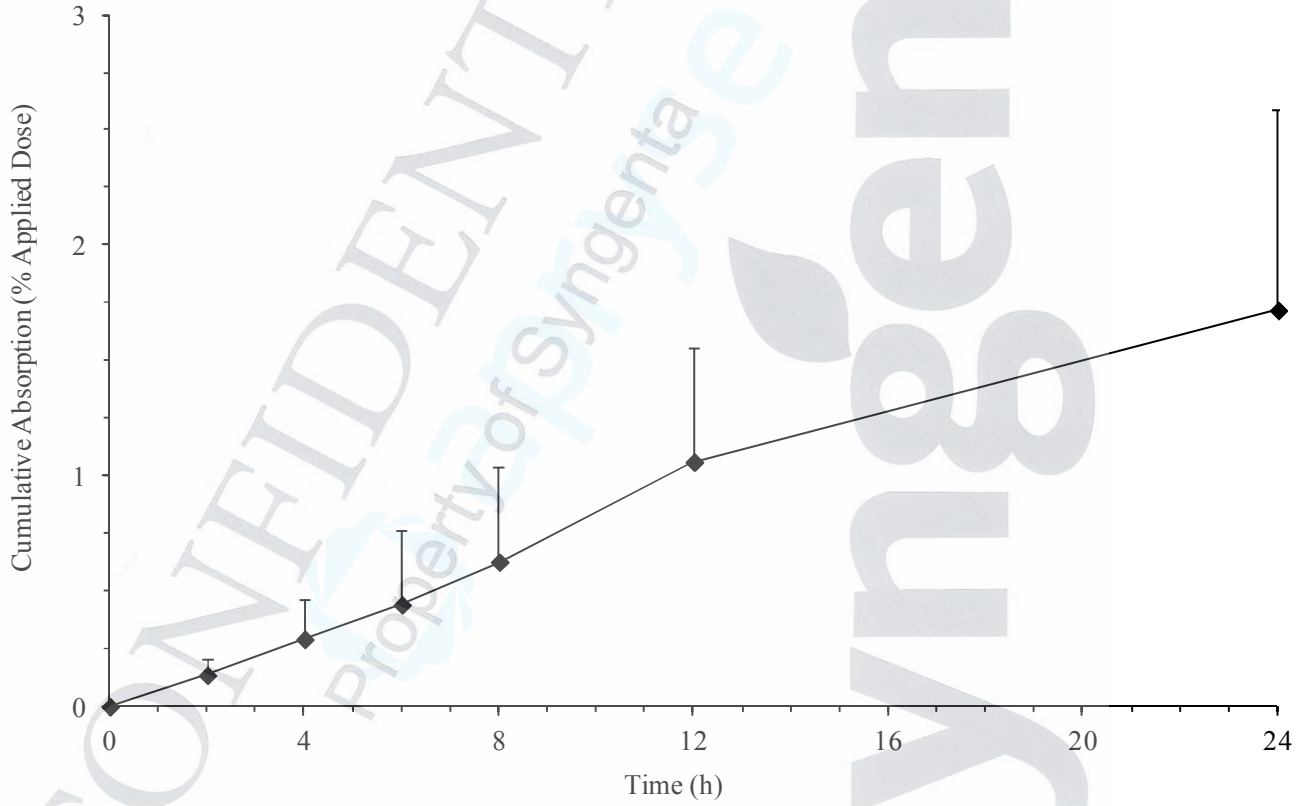

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FIGURE 19 Absorption Profile of [^{14}C]-Isopyrazam (µg equiv./cm^2) in Receptor Fluid Following Topical Application of [^{14}C]-Isopyrazam Spray Dilution 1 (Test Preparation 5, 1.25 g/L) to Human Split-Thickness Membranes (Mean + SD, n = 8)

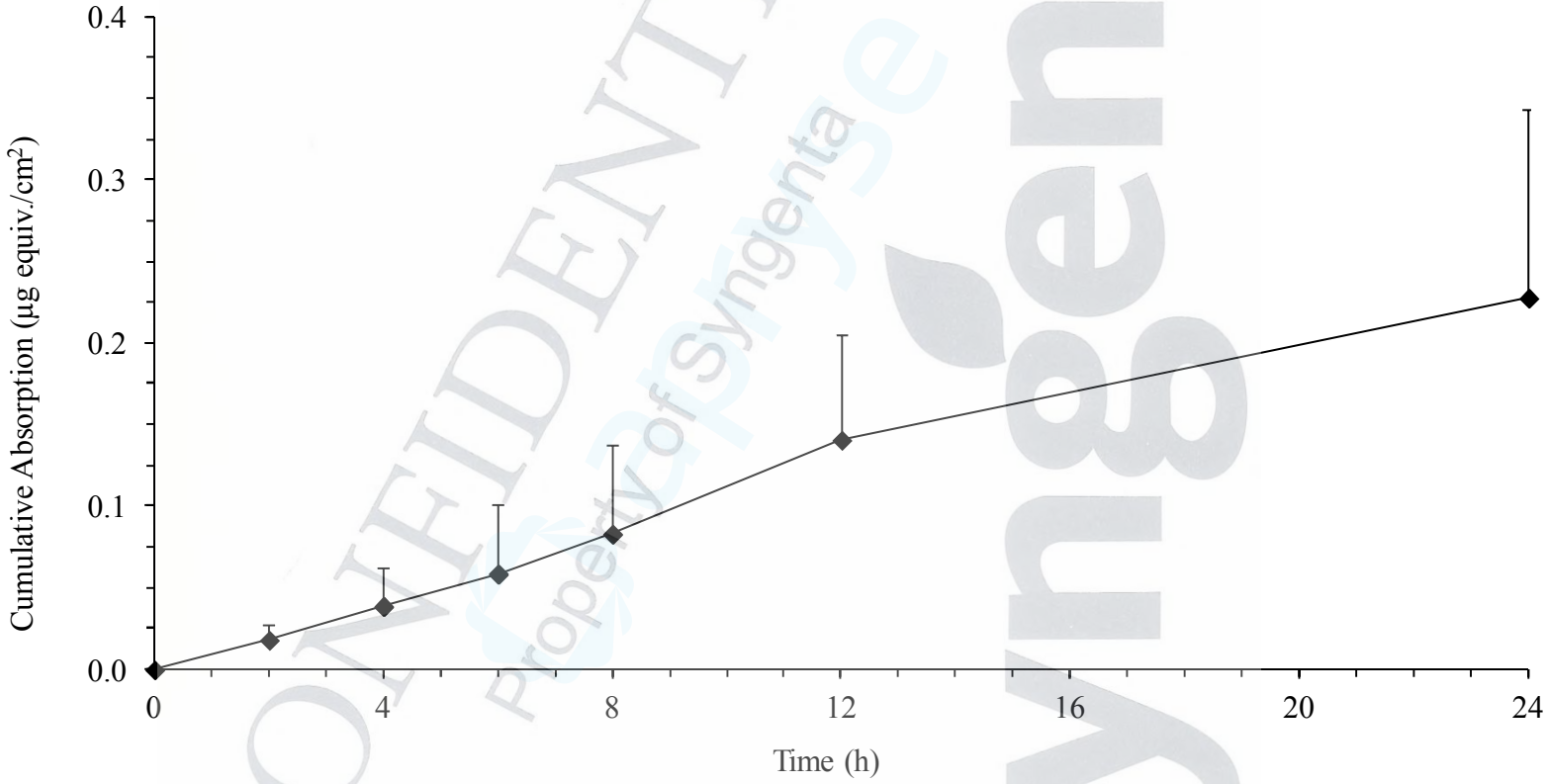

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FIGURE 20 **Distribution of [^{14}C]-Isopyrazam (µg equiv./cm^2) in the Stratum Corneum at 24 h Post Dose Following Topical Application of [^{14}C]-Isopyrazam Spray Dilution 1 (Test Preparation 5, 1.25 g/L) to Human Split-Thickness Membranes (Mean + SD, n = 8)**

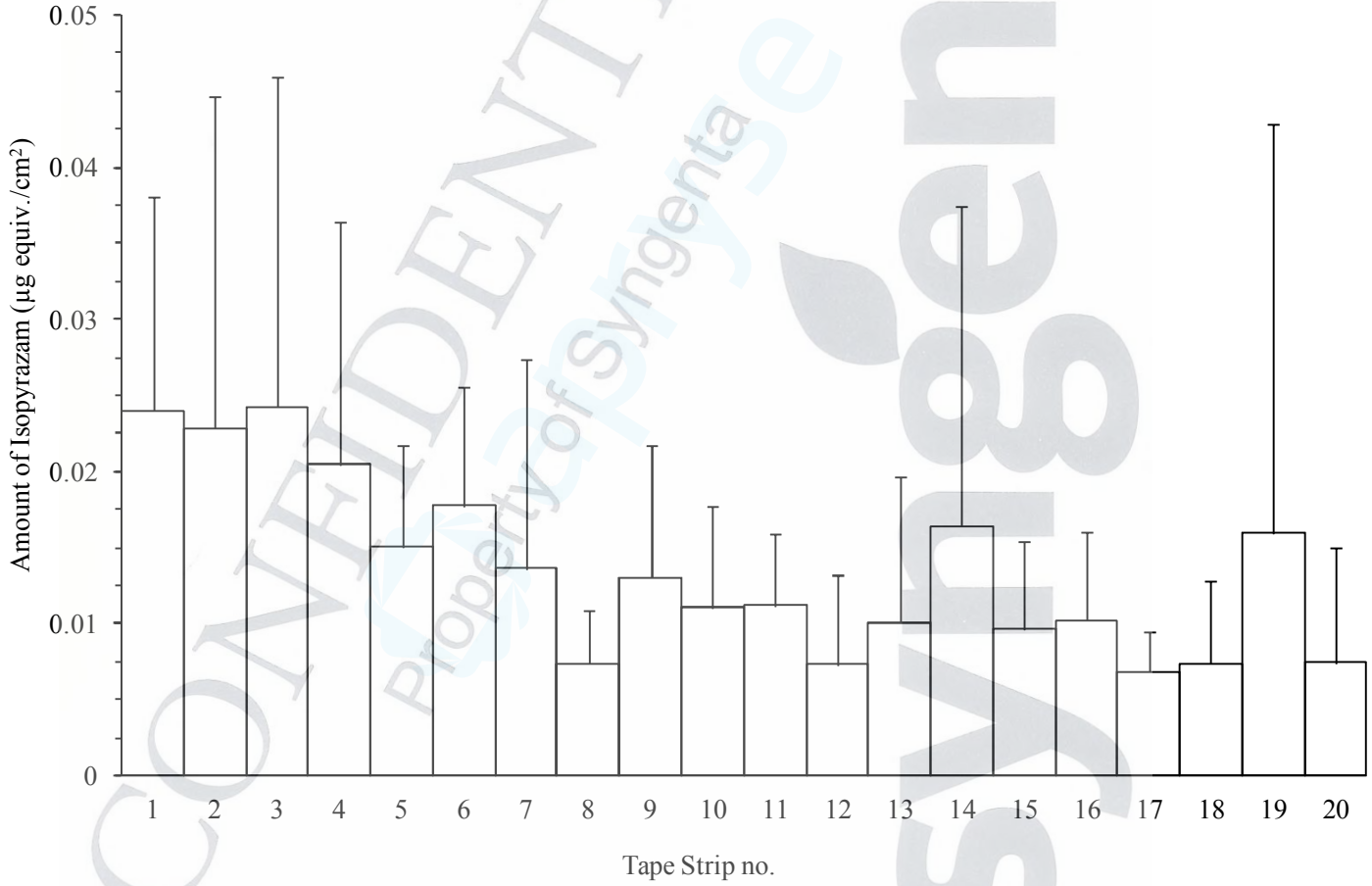

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FIGURE 21 Individual Absorption Profiles for [^{14}C]-Isopyrazam (% Applied Dose) in Receptor Fluid Following Topical Application of [^{14}C]-Isopyrazam Spray Dilution 2 (Test Preparation 6, 0.31 g/L) to Human Split-Thickness Membranes

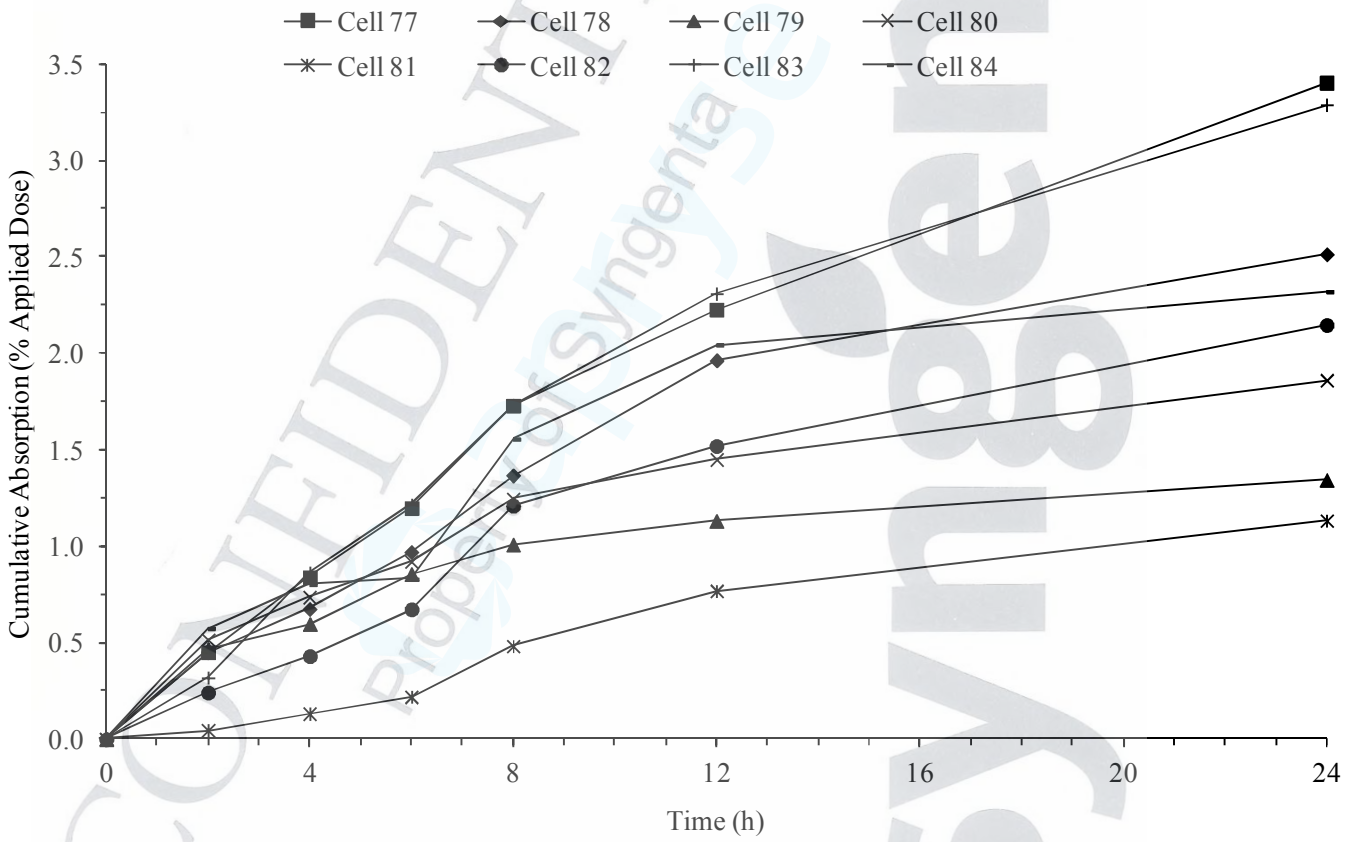

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FIGURE 22 Absorption Profile for [^{14}C]-Isopyrazam (% Applied Dose) in Receptor Fluid Following Topical Application of [^{14}C]-Isopyrazam Spray Dilution 2 (Test Preparation 6, 0.31 g/L) to Human Split-Thickness Membranes (Mean + SD, n = 8)

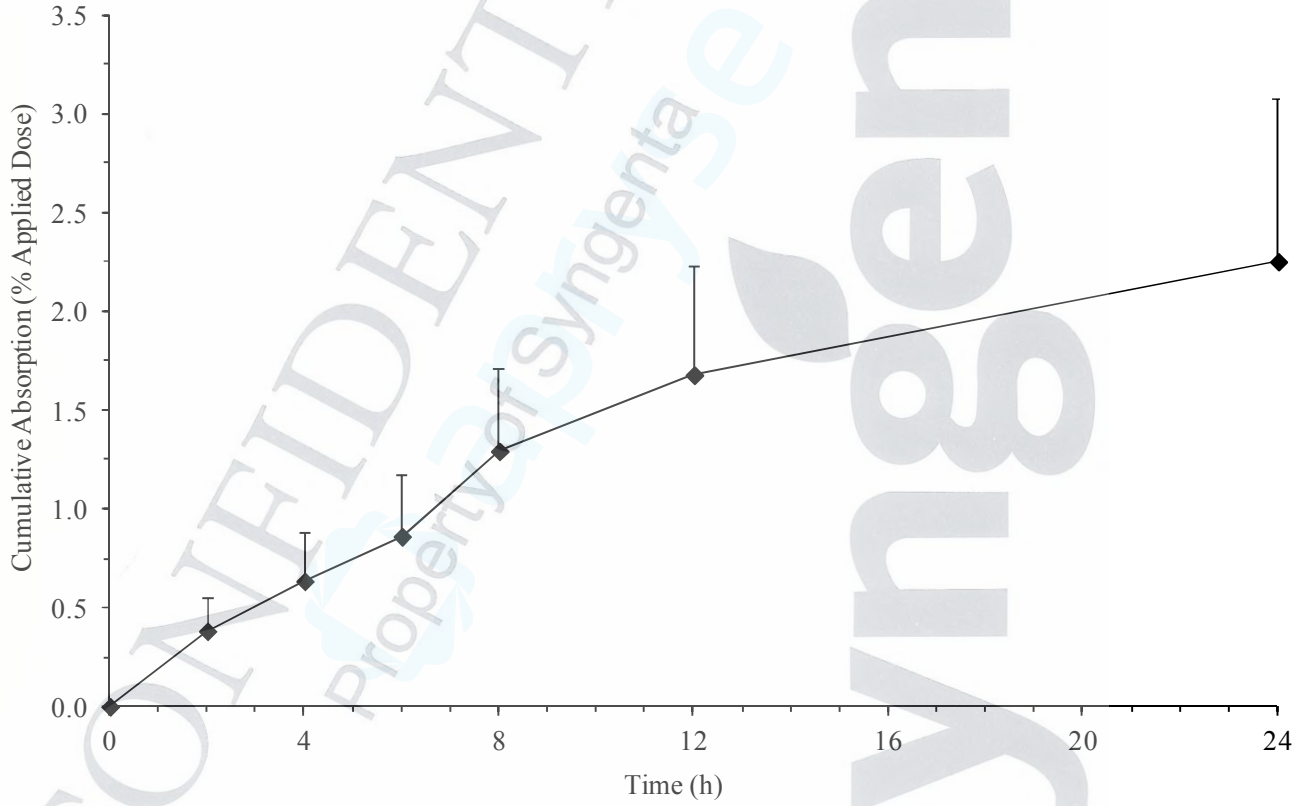

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FIGURE 23 Absorption Profile of [^{14}C]-Isopyrazam (µg equiv./cm^2) in Receptor Fluid Following Topical Application of [^{14}C]-Isopyrazam Spray Dilution 2 (Test Preparation 6, 0.31 g/L) to Human Split-Thickness Membranes (Mean + SD, n = 8)

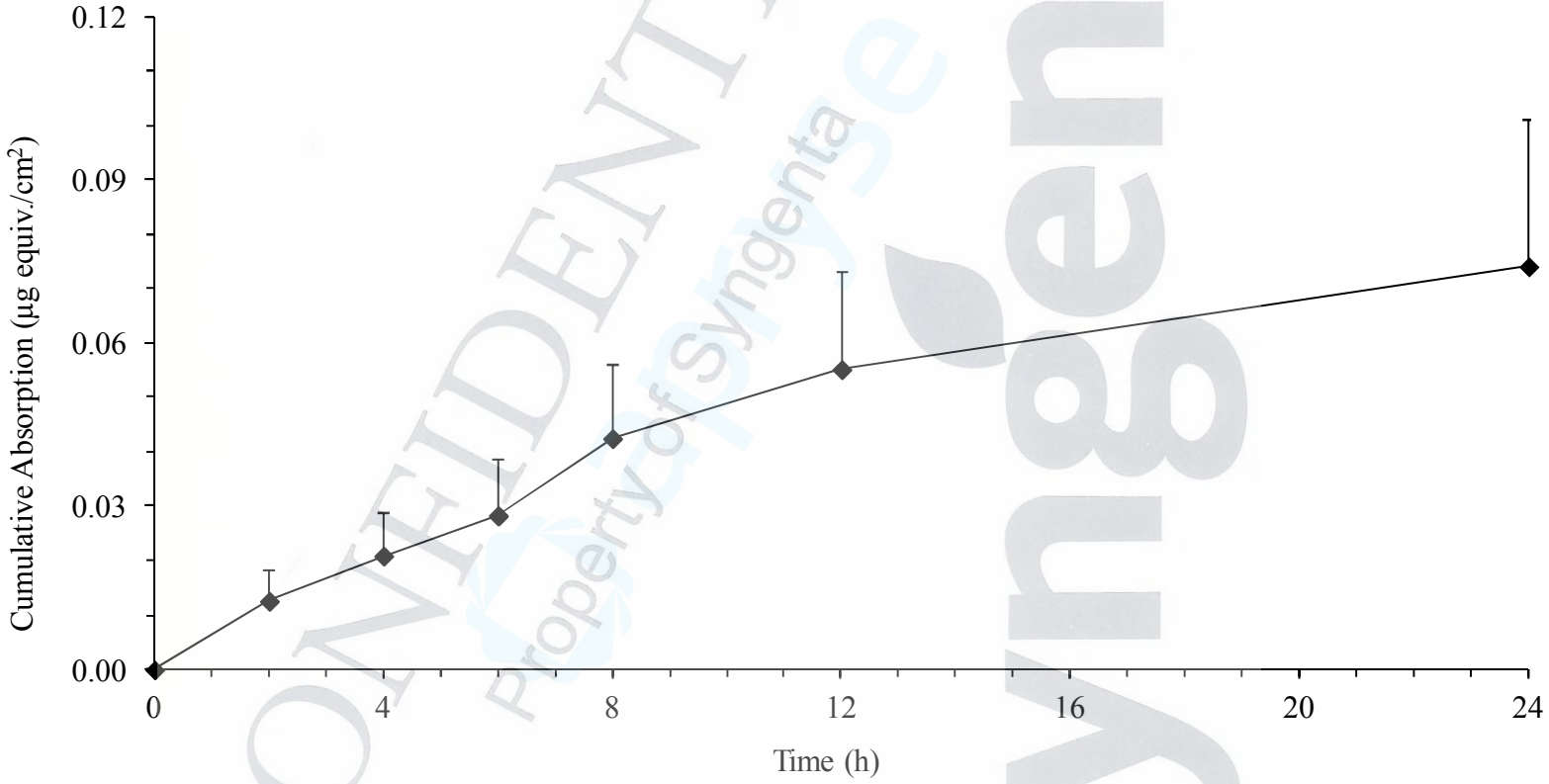

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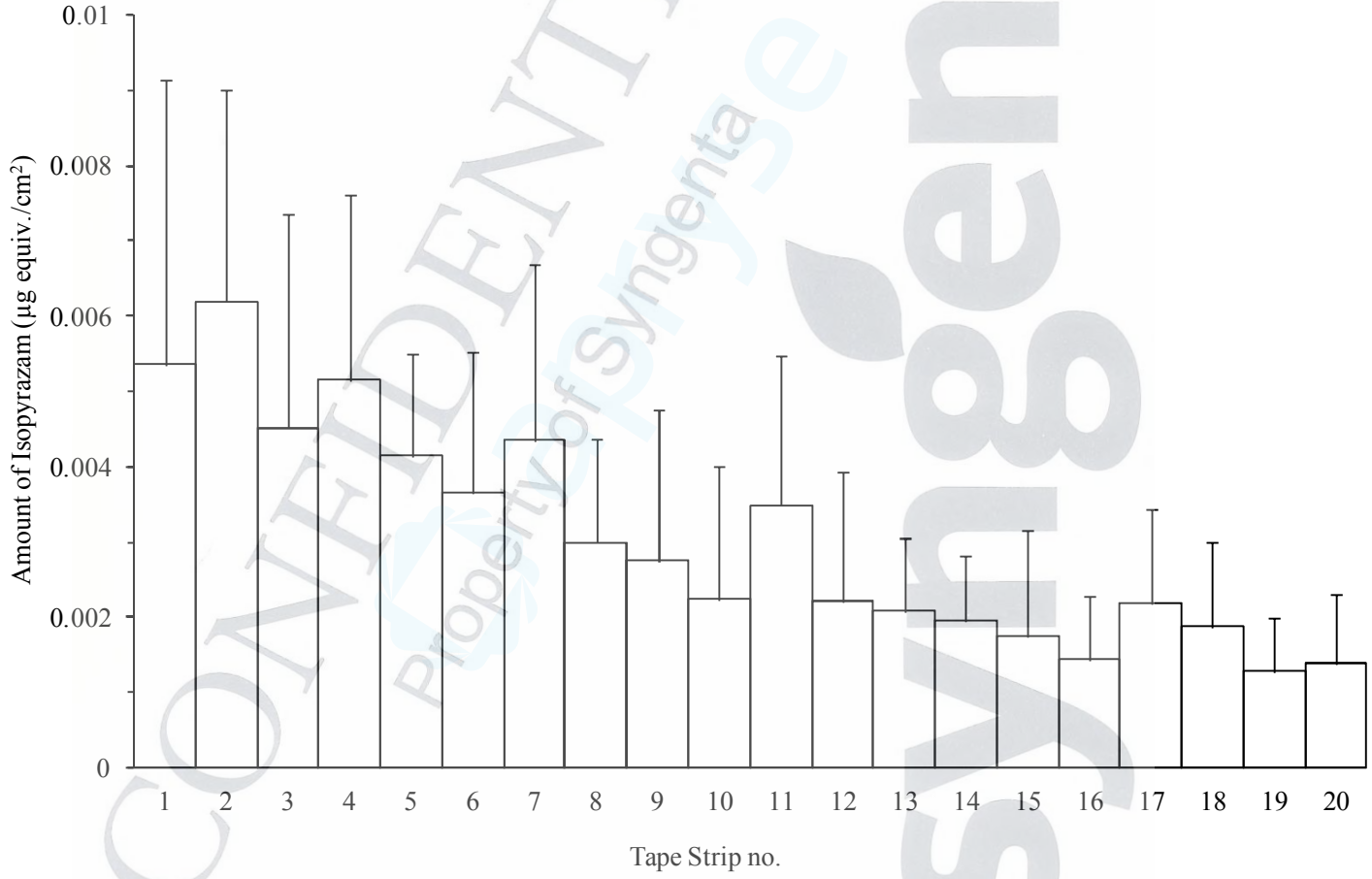
FIGURE 24 **Distribution of [^{14}C]-Isopyrazam (µg equiv./cm^2) in the Stratum Corneum at 24 h Post Dose Following Topical Application of [^{14}C]-Isopyrazam Spray Dilution 2 (Test Preparation 6, 0.31 g/L) to Human Split-Thickness Membranes (Mean + SD, n = 8)**



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APPENDICES SECTION

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APPENDIX 1 GLP Certificate

Department of Health

THE DEPARTMENT OF HEALTH OF THE GOVERNMENT OF THE UNITED KINGDOM

GOOD LABORATORY PRACTICE

STATEMENT OF COMPLIANCE
IN ACCORDANCE WITH DIRECTIVE 2004/9/EC

TEST FACILITY	TEST TYPE(S)
Charles River Laboratories Preclinical Services Elphinstone Research Centre Tranent Edinburgh EH33 2NE	Analytical/Clinical Chemistry Environmental Fate Environmental Toxicity Ecosystems Phys.Chem. Testing Residue Studies Mutagenicity Toxicology

DATE OF INSPECTION

19 June 2012

An inspection for compliance with the Principles of Good Laboratory Practice was carried out at the above 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 test facility was operating in compliance with the OECD Principles of Good Laboratory Practice.

This statement constitutes a Good Laboratory Practice Instrument (as defined in the UK Good Laboratory Practice Regulations 1999).

19/9/12

Dr. Andrew J. Gray
Head, UK GLP Monitoring Authority

MHRA

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

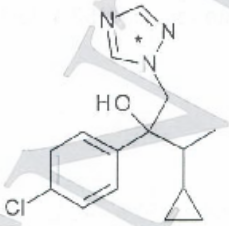
SYNGENTA CROP PROTECTION LLC
PRODUCT SAFETY NOAM / PRODUCT SAFETY OPERATIONS
GREENSBORO, NORTH CAROLINA, USA

CERTIFICATE OF ANALYSIS

SYNGENTA CODE: [TRIAZOLYL-U-14C]-SAN 619F

SYNONYMNS: [TRIAZOLYL-U-14C]-CSAA208793

REFERENCE NUMBER (Batch Identification): CDC-XXXIV-66-1



STRUCTURE: (* denotes universal ring radiolabel)

CHEMICAL PURITY: 99.4% (ISOMERS SUMMED)

ISOMER RATIO: 50.8 : 49.2

RADIOCHEMICAL PURITY: 99.3% (ISOMERS SUMMED)

SPECIFIC ACTIVITY: 57.3 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: May 31, 2013

STUDY COMPLETION DATE: November 28, 2012

STUDY DIRECTOR: William F. Helke

SIGNATURE: William F. Helke

CLASSIFICATION: PUBLIC

RESULTADOS DE TESTES E OUTROS DADOS NÃO DIVULGADOS
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APPENDIX 2
(Continued)

IDENTITY

- **COMPARISON TO AN AUTHENTIC STANDARD:**
  Reference: (data ref.: R12-53/4,5; test date: 11/28/12)

  Thin-Layer Chromatography Systems:

  Diol gel plate; Hexanes : Ethyl Acetate (1:3); Rf = 0.20 & 0.26 (two isomers)
  Silica gel plate; Chloroform : Isopropanol (9:1); Rf = 0.35 & 0.41 (two isomers)

- **SPECTRAL IDENTITY:**

MASS SPECTROSCOPY	:	Consistent with proposed structure. Reference: (data ref.: R12-53/4; test date: 11/27/12)

PURITY

CHEMICAL PURITY – AREA DISTRIBUTION BY HPLC	:	99.4% (isomer ratio: 50.8 : 49.2) Reference: (data ref.: R12-53/1,2,3; test date: 11/28/12)
RADIOCHEMICAL PURITY – AREA DISTRIBUTION BY THIN-LAYER CHROMATOGRAPHY		99.3% Reference: (data ref.: R12-53/4,5; test date: 11/28/12)

SPECIFIC ACTIVITY

SPECIFIC ACTIVITY – EXTERNAL STANDARD ANALYSIS BY HPLC		57.3 µCi/mg Reference: (data ref.: R12-53/1,2,3; test date: 11/28/12)

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

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

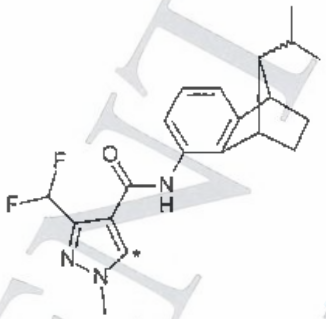
CERTIFICATE OF ANALYSIS

SYNGENTA CODE: [PYRAZOLYL-5-14C]-SYN 520453

SYNONYMNS: [PYRAZOLYL-5-14C]- CSCD602770

REFERENCE NUMBER (Batch Identification): CDC-XXXIV-56-1

STRUCTURE:



CHEMICAL PURITY: 99.5%

ISOMER RATIO: 85% SYN : 15% ANTI

RADIOCHEMICAL PURITY: 98.2%

SPECIFIC ACTIVITY: 63.3 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: May 31, 2013

STUDY COMPLETION DATE: November 9, 2012

STUDY DIRECTOR: William F. Helke

SIGNATURE: William F. Helke

CLASSIFICATION: PUBLIC

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APPENDIX 3
(Continued)

ANALYTICAL STANDARD
CHARACTERIZATION REPORT

IDENTITY

- **COMPARISON TO AN AUTHENTIC STANDARD:**
  Reference: (data ref.: R12-48/4,5; test date: 11/7/12)

  Thin-Layer Chromatography Systems:

  Silica gel plate: Hexane / Acetone (2:1); Rf = 0.28
  C8 gel plate; Acetonitrile / Isopropanol / Water (6:1:3); Rf = 0.39

- ***SPECTRAL IDENTITY:***

MASS SPECTROSCOPY	:	Consistent with proposed structure. Reference: (data ref.: R12-48/5; test date: 11/7/12)

PURITY

CHEMICAL PURITY – AREA DISTRIBUTION BY CAPILLARY HPLC	:	99.5% (ISOMERS SUMMED) 85% SYN : 15% ANTI Reference: (data ref.: R12-48/1,2,3; test date: 11/8/12)
RADIOCHEMICAL PURITY – AREA DISTRIBUTION BY THIN-LAYER CHROMATOGRAPHY		98.2% Reference: (data ref.: R12-48/4,5; test date: 11/7/12)

SPECIFIC ACTIVITY

SPECIFIC ACTIVITY – EXTERNAL STANDARD ANALYSIS BY HPLC	63.3 µCi/mg Reference: (data ref.: R12-48/1,2,3; test date: 11/8/12)

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APPENDIX 4 Certificate of Analysis for Non Radiolabelled Test Items

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Syngenta Crop Protection, LLC
Technology & Projects
Analytical & Product Chemistry
Greensboro, NC 27409

Certificate of Analysis

Cyproconazole Technical
Batch ID 612042 (CZ602108)

Batch Identification	612042
Product Design Code	SAN619A
Product by Common Name	Cyproconazole
Source	Syngenta LLC., Omaha, NE
Other ID	CZ602108

Chemical Analysis
(Active Ingredient Content)

Identity of the Active Ingredient*	Confirmed
Content of Cyproconazole Technical*	98.3% (wt/wt)

Methodology Used for Characterization: LC
The Active Ingredient content is within the FAO limits.

Physical Analysis

Appearance*	white powder

Stability

Storage Temperature	< 30°C
Recertification date	End of January 2014

If stored under the conditions given above, this test substance can be considered stable until the recertification date is reached.

The stability of this test substance will be determined concurrently through reanalysis of material held in inventory under GLP conditions at Syngenta Crop Protection, LLC, Greensboro, NC.

This Certificate of Analysis is summarizing data (marked with an asterisk) from a study that has been performed in compliance with Good Laboratory Practices per 40 CFR Part 160. Raw data, documentation, protocols, any amendments to study protocols and reports pertaining to this study are maintained in the Syngenta Crop Protection Archives in Greensboro, NC.

Authorization:

Nancy Liu
Team Leader
Analytical & Product Chemistry Department

Feb 23, 2011
Date

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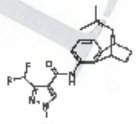
GLP Testing Facility WMU
Analytical Development &
Product Chemistry GS2131

Syngenta Crop Protection
Münchwilen AG
Breitenloh 5
CH-4333 Münchwilen

Certificate of Analysis

Isopyrazam tech.



SMO0A037/1 - Purity 97.1 % w/w

Batch Identification	**SMO0A037/1**
Product Code	**Isopyrazam tech.**
Other Product Code(s)	SYN520453 tech.
CA Reg. No.	881685-58-1
CA Index Name	1H-pyrazole-4-carboxamide, 3-(difluoromethyl)-1-methyl-N-[1,2,3,4-tetrahydro-9-(1-methylethyl)-1,4-methanonaphthalen-5-yl]
IUPAC Name	3-difluoromethyl-1-methyl-1H-pyrazole-4-carboxylic acid (9-isopropyl-1,2,3,4-tetrahydro-1,4-methano-naphthalen-5-yl)-amide
Molecular formula	$C_{20}H_{23}F_2N_3O$
Molecular mass	359.4
Chemical Analysis	
– **Identity ***	**confirmed**
– **Content of Isopyrazam ***	**97.1 % w/w**
– **Content of SYN534969 * (syn-epimer)**	**82.9 % w/w**
– **Content of SYN534968 * (anti-epimer)**	**14.2 % w/w**
Methodology used for Characterization	HPLC
Physical Analysis	
– **Appearance ***	**Off-white powder**
Stability:	
– **Storage Temperature**	**< 30°C**
– **Reanalysis Date**	**End of November 2014**

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

This Certificate of Analysis is summarizing data which originate either from a single study or from several individual studies which have been performed in compliance with GLP. Tests marked with an asterisk (*) have been conducted within a single study/as individual studies. Raw data, documentation, study plans, any amendments to study plans and reports pertaining to this/these studie(s) are stored under the study number(s) referenced below within the archives of the GLP Testing Facility WMU at Syngenta Crop Protection Münchwilen AG.

Characterization: 122083

Authorisation:

26 November 2010

Dr. R. Kellner
Analytical Development & Product Chemistry

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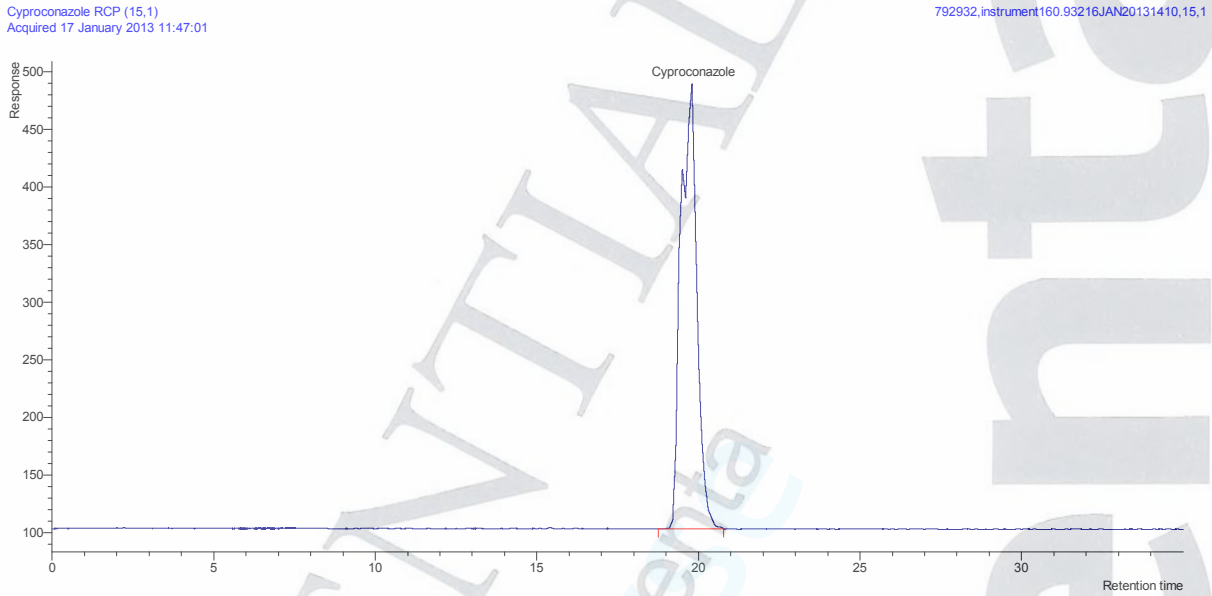
APPENDIX 5 HPLC Chromatogram for Radiochemical Purity of [^{14}C]-Cyproconazole



Retention Time (min)	Peak Area (%)
19.80	100

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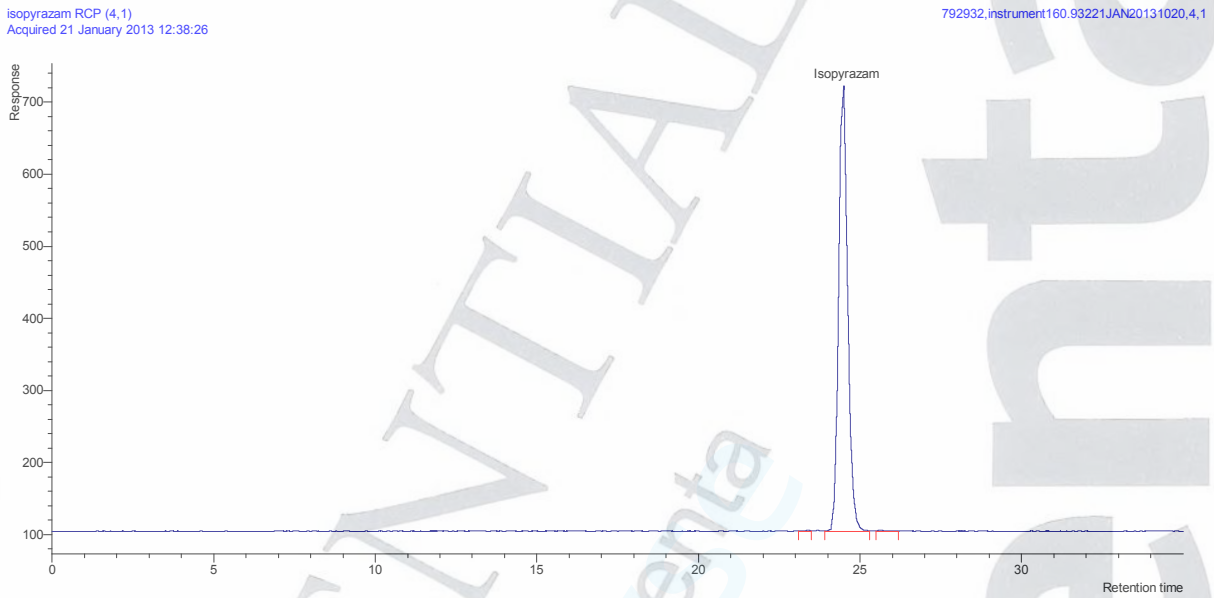
APPENDIX 6 HPLC Chromatogram for Radiochemical Purity of [^{14}C]-Isopyrazam



Retention Time (min)	Peak Area (%)
23.40	0.2
24.50	99.6
25.60	0.2

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APPENDIX 7 Human Skin Donor Details

Charles River Donor No.	Sex/Age	Site	Supplier
0401	M/48Y	Abdomen + Breast	NHS Lothian
0403	F/32Y	Abdomen	NHS Lothian
0410	F/33Y	Abdomen	NHS Lothian
0420	F/43Y	Abdomen	NHS Lothian
0444	F/34Y	Abdomen	Tissue Solutions
0445	F/62Y	Abdomen + Thigh	Tissue Solutions

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APPENDIX 8 Thickness of Full and Split-Thickness Skin Membranes

Charles River Donor No.	Membrane Thickness (µm)	
	Full Thickness Skin	Split-Thickness Skin
0401	1800-2090	400
0403	1250-1820	390-400
0410	600-1300	380-390
0420	1120-1380	360-390
0444	1130-1150	400
0445	1650-1760	390-400

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APPENDIX 9 Cross Reference of Cell Number with Donor Number and Electrical Resistance

Cell Number	Charles River Donor No.	Electrical Resistance (kΩ)
37	0403	15.13
38	0403	14.89
39	0410	19.67
40	0410	20.78
41	0401	20.56
42	0401	20.26
43	0444	19.38
44	0444	18.57
45	0403	15.39
46	0403	19.41
47	0410	13.73
48	0410	19.77
49	0401	16.11
50	0401	15.41
51	0444	14.30
52	0444	22.30
53	0403	15.79
54	0403	15.04
55	0410	15.18
56	0410	14.23
57	0401	18.46
58	0401	14.45
59	0444	20.01
60	0444	18.82
61	0401	15.52
62	0401	15.94
63	0410	18.86
64	0410	15.84
65	0420	20.23
66	0420	18.47
67	0445	19.67
68	0445	14.26
69	0401	20.96
70	0401	20.81
71	0410	19.37
72	0410	20.44
73	0420	20.03
74	0420	15.11
75	0445	20.68
76	0445	19.82
77	0401	16.11
78	0401	18.94
79	0410	20.63
80	0410	15.82
81	0420	20.79
82	0420	19.81
83	0445	21.08
84	0445	19.74

Rejection criterion, sample rejected if electrical resistance < 4 kΩ for split-thickness skin.

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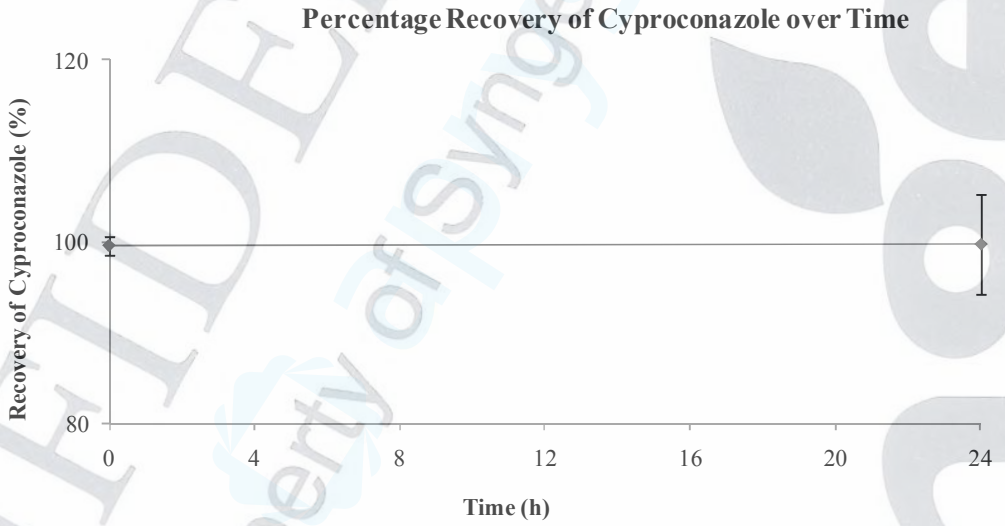
APPENDIX 10 Recovery of Radioactivity (% Applied dose) Following Topical Application of Test Preparation to Aluminium Foil for a Volatility Assessment

[^{14}C]-Cyproconazole in Formulation Concentrate (Test Preparation 1, 80 g/L)

	Cell Number and Termination Time					
	0 h			24 h		
	Cell 1	Cell 2	Cell 3	Cell 4	Cell 5	Cell 6
Donor Wash and Foil	98.71	100.64	99.39	96.05	97.02	106.12
Mass Balance	98.71	100.64	99.39	96.05	97.02	106.12
Mean Mass Balance	99.58			99.73		
SD	0.98			5.56		



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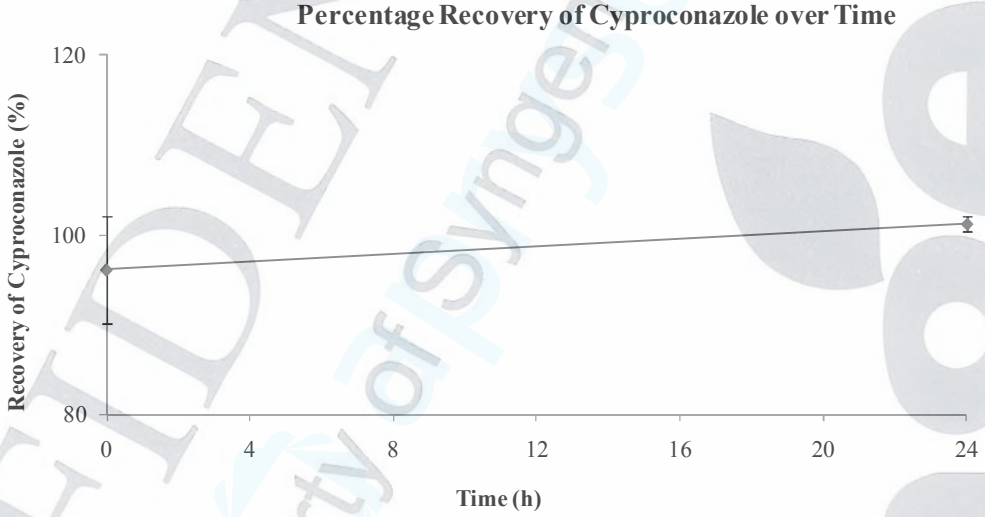
[^{14}C]-Cyproconazole in Spray Dilution 1 (Test Preparation 2, 0.8 g/L)

	Cell Number and Termination Time					
	0 h			24 h		
	Cell 7	Cell 8	Cell 9	Cell 10	Cell 11	Cell 12
Donor Wash and Foil	97.39	101.39	89.68	100.79	102.19	100.74
Mass Balance	97.39	101.39	89.68	100.79	102.19	100.74
Mean Mass Balance	96.15			101.24		
SD	5.95			0.82		



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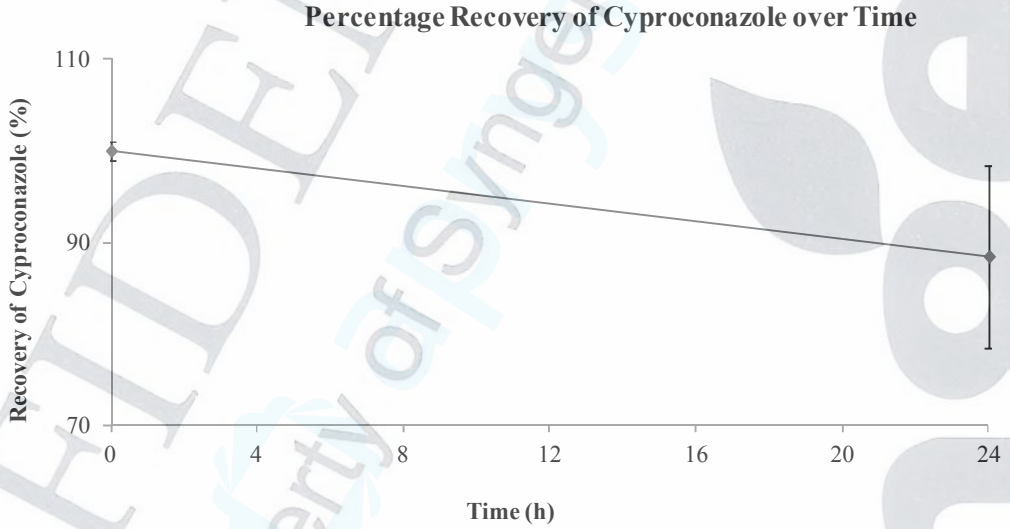
[^{14}C]-Cyproconazole in Spray Dilution 2 (Test Preparation 3, 0.2 g/L)

	Cell Number and Termination Time					
	0 h			24 h		
	Cell 13	Cell 14	Cell 15	Cell 16	Cell 17	Cell 18
Donor Wash and Foil	99.49	101.15	99.24	93.12	95.20	76.94
Mass Balance	99.49	101.15	99.24	93.12	95.20	76.94
Mean Mass Balance	99.96			88.42		
SD	1.04			10.00		



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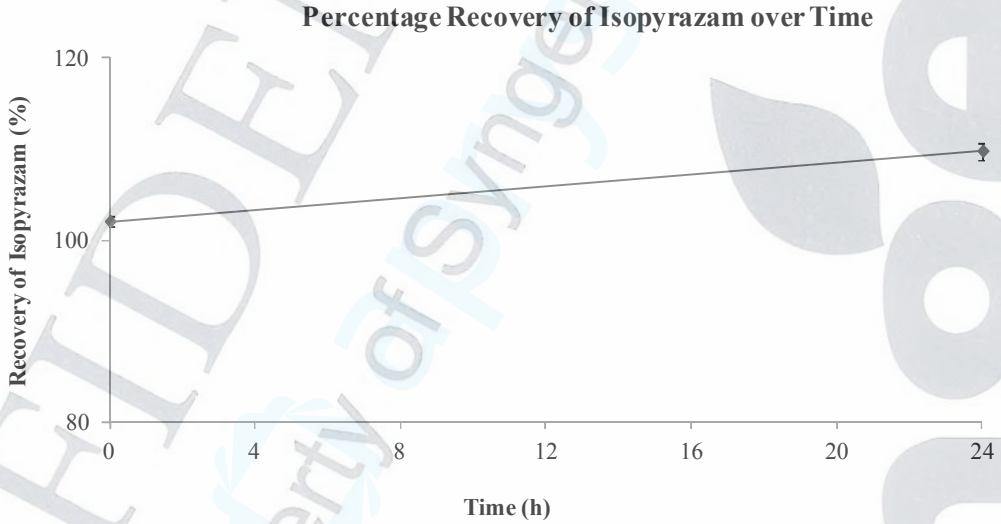
[^{14}C]-Isopyrazam in Formulation Concentrate (Test Preparation 4, 125 g/L)

	Cell Number and Termination Time					
	0 h			24 h		
	Cell 19	Cell 20	Cell 21	Cell 22	Cell 23	Cell 24
Donor Wash and Foil	101.78	102.63	101.67	110.54	110.03	108.70
Mass Balance	101.78	102.63	101.67	110.54	110.03	108.70
Mean Mass Balance	102.03			109.76		
SD	0.53			0.95		



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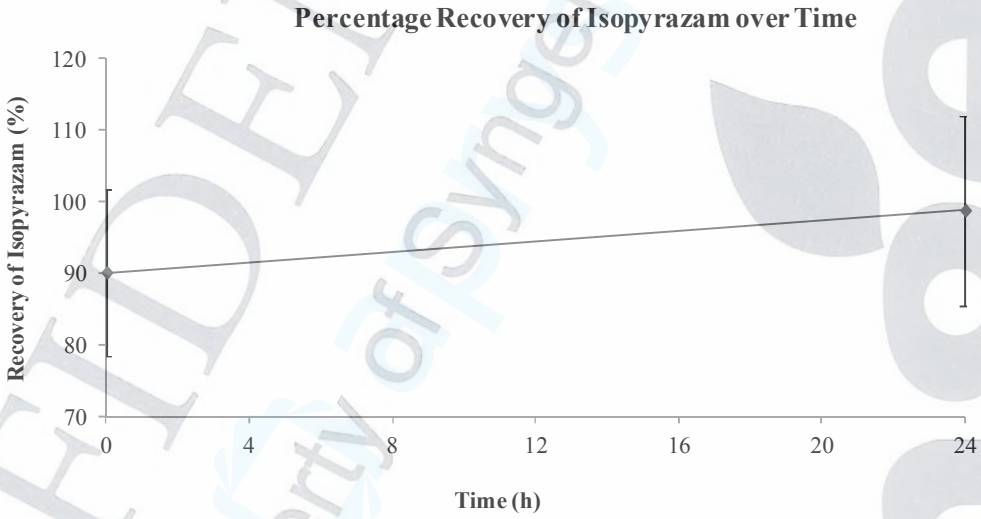
[^{14}C]-Isopyrazam in Spray Dilution 1 (Test Preparation 5, 1.25 g/L)

	Cell Number and Termination Time					
	0 h			24 h		
	Cell 25	Cell 26	Cell 27	Cell 28	Cell 29	Cell 30
Donor Wash and Foil	98.60	76.85	94.87	106.78	106.21	83.43
Mass Balance	98.60	76.85	94.87	106.78	106.21	83.43
Mean Mass Balance	90.11			98.81		
SD	11.63			13.32		



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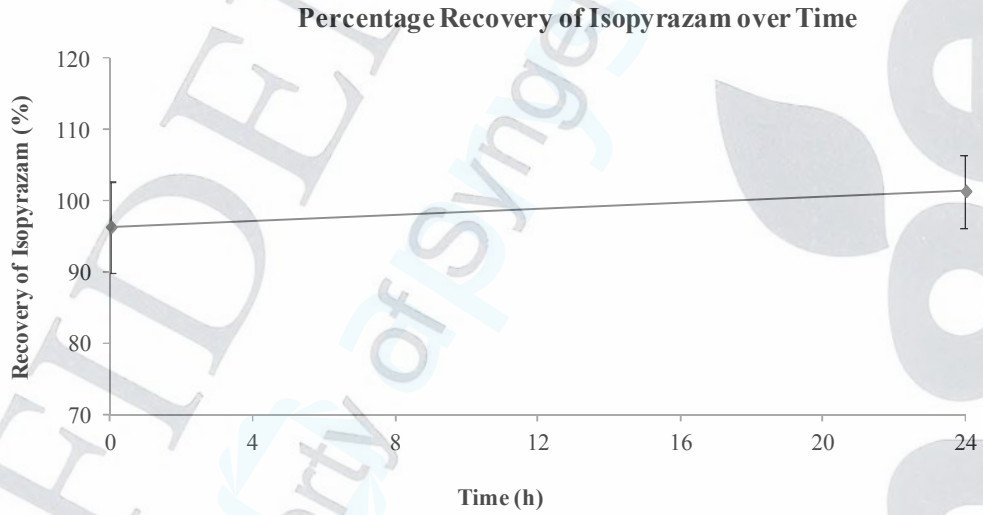
[^{14}C]-Isopyrazam in Spray Dilution 2 (Test Preparation 6, 0.31 g/L)

	Cell Number and Termination Time					
	0 h			24 h		
	Cell 31	Cell 32	Cell 33	Cell 34	Cell 35	Cell 36
Donor Wash and Foil	98.33	89.20	101.37	104.51	104.12	95.42
Mass Balance	98.33	89.20	101.37	104.51	104.12	95.42
Mean Mass Balance	96.30			101.35		
SD	6.33			5.14		



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APPENDIX 11 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.

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APPENDIX 11
(Continued)

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.

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