Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods.

Liquid chromatography tandem mass spectrometric assay methods were developed and validated to support the analysis of clinical study samples. All the assays were developed with the aim of high sensitivity (lower than 0.5 ng/ml) with reliable quantitation. While optimizing the lower limit of quantitation (LLOQ) of each analyte, various parameters like signal to noise, accuracy, and precision were evaluated and LLOQ was set as 0.20, 0.40, 0.40, and 0.20 ng/mL for avobenzone, oxybenzone, octocrylene and ecamsule, respectively. The upper limit of quantitation (ULOQ) of oxybenzone was selected based on the exposure data available in literature [1] and was set at 300 ng/mL. However, there was no, or limited exposure data reported for avobenzone, octocrylene, or ecamsule. However, there was no, or limited, exposure data reported for avobenzone, octocrylene, or ecamsule. Therefore, the ULOQ of avobenzone, octocrylene, and ecamsule was selected based on the concentration at which acceptable linearity range was observed (i.e., concentration vs linear detector response) and was set as 12, 20, and 10 ng/mL, respectively. The details of individual methods and validation parameters are described below.

eMethods 1. Bioanalytical Method Conditions for Avobenzone and Oxybenzone

Validation range:	0.2–12 ng/mL for Avobenzone and 0.4–300 ng/mL for Oxybenzone
High Performance Liquid Chromatography (HPLC) instrument:	Agilent 1290 Infinity
Mass Spectrometer:	AB SCIEX 6500^+ Mass spectrometer
HPLC Conditions	
Mobile Phase:	10 mM Ammonium formate with 0.1% Formic acid in water and methanol (24: 76, v/v)
Flow rate:	0.7 mL/min
Column:	Acquity UPLC® BEH Shield RP18 (2.1 x 50 mm) 1.7 µm
Injection Volume:	5 µL
Retention Time:	Avobenzone and Avobenzone-d_3: 2.00 minute Oxybenzone and Oxybenzone-d_3: 0.50 minute
Run Time:	3.0 minutes
Mass Spectrometer conditions	
Ionization Source and scan type:	Atmospheric Pressure Chemical Ionization (APCI); Multiple Reaction Monitoring (MRM)
Data acquisition:	Analyst 1.6.3

AB SCIEX 6500^+ Q-TRAP mass spectrometer state file parameters:

Parameter	**Avobenzone**	**Avobenzone–d_3 (IS1)**	**Oxybenzone**	**Oxybenzone–d_3 (IS2)**
Q1 mass/Q3 mass (amu)	311.2/161.2	314.2/161.2	229.2/151.2	232.2/154.1
Declustering potential, V	100	100	100	100
Collision Energy (V)	31	31	25	27
Collision Cell Exit Potential (V)	11	11	11	11
Source Temperature (^{0} C):	500	500	500	500
Collision Gas (CAD)	Medium	Medium	Medium	Medium
Curtain Gas (CUR)	40	40	40	40
Ion Source Gas 1 (GS1)	50	50	50	50
Nebulizer Current	3	3	3	3

Sample Preparation for Avobenzone and Oxybenzone: A 150 µL aliquot of the sample was added to Phree Phospholipid removal 96-well plates (Make: Phenomenex, Part no 8E-S133-TGB) and treated with 500 µL of

acetonitrile containing 4.00 ng/mL of internal standard-1 (Avobenzone-d_3) and 10.00 ng/mL of internal standard-2 (Oxybenzone-d_3). The samples were vortexed for 4 min, followed by centrifugation at 5 *g* for 5 min. Then, 100µL of the filtrate was transferred to 96-well collection plates, 50µL of 10mM ammonium formate in 0.1% formic acid was added, and plates were shaken for 1 minute.

Validation Summary Table for Avobenzone and Oxybenzone

Description	**Avobenzone**	**Oxybenzone**
Short description of method	Protein precipitation with Phospholipid removal plates Reverse-phase HPLC with tandem mass spectrometric detection	Protein precipitation with Phospholipid removal plates Reverse-phase HPLC with tandem mass spectrometric detection
Biological matrix	Human plasma (dipotassium ethylenediaminetetraacetic acid)	Human plasma (dipotassium ethylenediaminetetraacetic acid)
Analyte	Avobenzone	Oxybenzone
Internal standard (IS)	Avobenzone –d_3	Oxybenzone–d_3
Calibration concentrations	0.20 ng/mL to 12.00 ng/mL	0.40 ng/mL to 300.00 ng/mL
QC concentrations	0.20 ng/mL, 0.60 ng/mL, 1.50 ng/mL, 6.00 ng/mL and 10.00 ng/mL	0.40 ng/mL, 1.20 ng/mL, 40.00 ng/mL, 150.00 ng/mL, and 260.00 ng/mL
Selectivity	No significant interference observed in the 16 blank matrix lots screened.	No significant interference observed in the 16 blank matrix lots screened.
Specificity	No significant interference observed.	No significant interference observed.
Lower limit of quantitation	0.20 ng/mL Between-run accuracy 108% Between-run precision 11% Within-run accuracy 108% Within-run precision 9%	0.40 ng/mL Between-run accuracy 101% Between-run precision 11% Within-run accuracy 111% Within-run precision 5%
Between-run accuracy	94% to 104%	96% to 101%
Between-run precision	4% to 9%	2% to 8%
Within-run accuracy	91% to 104%	95% to 105%
Within-run precision	3% to 8%	1% to 6%
IS normalized matrix factor	LQC: 1.13 (%CV: 3) HQC: 1.00 (%CV: 3)	LQC: 1.12 (%CV: 7) HQC: 1.02 (%CV: 1)
Dilution integrity	Concentration 36.00 ng/mL Diluted 5-fold: Accuracy 103%, Precision 4% Diluted 10-fold: Accuracy 104%, Precision 4%.	Concentration 900.00 ng/mL Diluted 5-fold: Accuracy 99%, Precision 2% Diluted 10-fold: Accuracy 100%, Precision 2%
Recovery of analyte	76% -85%	98% -105%
Recovery of IS	81%	90%
Auto-sampler storage stability	Confirmed up to 35 hours at 5°C nominal Accuracy 107% for LQC and 99% for HQC	Confirmed up to 35 hours at 5°C nominal Accuracy 97% for LQC and 100% for HQC
Freeze thaw stability	Confirmed up to five cycles Accuracy 103% for LQC and 106% for HQC	Confirmed up to five cycles Accuracy 112% for LQC and 104% for HQC

Description	Avobenzone	Oxybenzone
Bench top stability	Confirmed up to 15 hours at 24°C nominal Accuracy 104% for LQC and 111% for HQC	Confirmed up to 15 hours at 24°C nominal Accuracy 113% for LQC and 105% for HQC
Stock solution stability	Confirmed up to 90 days at -20°C nominal. %Stability 102%	Confirmed up to 90 days at -20°C nominal. %Stability 101%
Injector Carryover	Not significant (not detected)	Not significant (not detected)
Co-administration drug effect	Accuracy LQC: 113% Accuracy HQC: 107%	Accuracy LQC: 101% Accuracy HQC: 103%
Long term Stability in Plasma	Confirmed up to 187 days at -80°C nominal % Stability 104% for LQC and 99% for HQC	Confirmed up to 187 days at -80°C nominal % Stability 96% for LQC and 100% for HQC
QC: Quality control; LQC: Low quality control; HQC: High quality control; CV: Coefficient of variance		

eMethods 2. Bioanalytical Method Conditions for Octocrylene

Validation range:	0.4–20 ng/mL
High Performance Liquid Chromatography (HPLC) instrument:	Agilent 1290 Infinity
Mass Spectrometer:	AB SCIEX 6500^{+} Mass spectrometer

HPLC Conditions

Mobile Phase:	10 mM Ammonium formate with 0.1% Formic acid in water and methanol (15: 85, v/v)
Flow rate:	0.4 mL/min
Column:	Acquity UPLC® BEH Shield RP18 (2.1 x 50 mm) 1.7 µm
Injection Volume:	5 µL
Retention Time:	Octocrylene and Octocrylene -d_{15}: 0.9 minute
Run Time:	2.0 minutes

Mass Spectrometer conditions

Ionization Source and scan type:	Atmospheric Pressure Chemical Ionization (APCI); Multiple Reaction Monitoring (MRM)
Data acquisition:	Analyst 1.6.3

AB SCIEX 6500^{+} Q-TRAP mass spectrometer state file parameters:

Parameter	**Octocrylene Ammonium adduct**	**Octocrylene –d_{15}**
Q1 mass/Q3 mass (amu)	379.0/250.0	377.1/251.1
Declustering potential, V	50	60
Collision Energy (V)	15	15
Collision Cell Exit Potential (V)	11	11
Source Temperature (^{0} C):	500	500
Collision Gas (CAD)	Medium	Medium
Curtain Gas (CUR)	40	40
Ion Source Gas 1 (GS1)	50	50
Nebulizer Current	3	3

Sample Preparation Octocrylene: 150 µL of acetonitrile containing 20 ng/mL of octocrylene-d_{15} was added to MultiScreen® solvinert protein precipitation 96-well plates (0.45µm, Low-Binding, Hydrophilic) (Make: Merck, Part no MSRLN0450) and a 50 µL aliquot of plasma sample was added to each well. The samples were vortexed for 5 min, followed by centrifugation at 4000 rpm for 5 min. Then, 50µL of 10mM ammonium formate in 0.1% formic acid was added and plates were shaken for 1 minute.

Validation Summary Table for Octocrylene

Description	**Octocrylene**
Short description of method	Protein precipitation with 96-well plates Reverse-phase HPLC with tandem mass spectrometric detection
Biological matrix	Human plasma (dipotassium ethylenediaminetetraacetic acid)
Analyte	Octocrylene
Internal standard (IS)	Octocrylene $-d_{15}$
Calibration concentrations	0.40 ng/mL to 20.00 ng/mL
QC concentrations	0.40 ng/mL, 1.20 ng/mL, 3.00 ng/mL, 10.00 ng/mL and 18.00 ng/mL
Selectivity	No significant interference observed in the 10 blank matrix lots screened.
Specificity	No significant interference observed.
Lower limit of quantitation	0.40 ng/mL Between-run accuracy 101% Between-run precision 14% Within-run accuracy 105% Within-run precision 9%
Between-run accuracy	98% to 104%
Between-run precision	6% to 9%
Within-run accuracy	101% to 104%
Within-run precision	3% to 7%
IS normalized matrix factor	LQC: 0.93 (%CV: 13) HQC: 1.04 (%CV: 5)
Dilution integrity	Concentration 60.00 ng/mL Diluted 5-fold: Accuracy 104%, Precision 5% Diluted 10-fold: Accuracy 111%, Precision 4%
Recovery of analyte	91% -102%
Recovery of IS	107%
Auto-sampler storage stability	Confirmed up to 36 hours at 5°C nominal. Accuracy 103% for LQC and 98% for HQC
Freeze thaw stability	Confirmed up to seven cycles, Accuracy 90% for LQC and 98% for HQC
Bench top stability	Confirmed up to 15 hours at 24°C nominal. Accuracy 88% for LQC and 88% for HQC
Stock solution stability	Confirmed up to 45 days at -20°C nominal. %Stability 97%
Injector Carryover	Not significant (not detected)
Co-administration drug effect	Accuracy LQC: 109% Accuracy HQC: 103%
Long term Stability in Plasma	Confirmed up to 168 days at -80°C nominal % Stability 103% for LQC and 87% for HQC
QC: Quality control; LQC: Low quality control; HQC: High quality control; CV: Coefficient of variance	

eMethods 3. Bioanalytical Method Conditions for Ecamsule

Validation range:	0.2–10 ng/mL
High Performance Liquid Chromatography (HPLC) instrument:	Agilent 1290 Infinity
Mass Spectrometer:	AB SCIEX 6500^{+} Mass spectrometer

HPLC Conditions

Mobile Phase A:	10 mM Ammonium Formate with 0.1% Formic acid in water
Mobile Phase B:	Acetonitrile

Gradient Table:

Time (Min)	Flow (mL/min)	A	B
0.0	0.6	90	10
0.3	0.6	90	10
0.4	0.6	20	80
1.0	0.6	10	90
1.8	0.6	10	90
2.0	0.6	90	10
2.5	0.6	90	10

Column:	Acquity UPLC® HSS T3 (2.1 x 100 mm) 1.8 µm
Injection Volume:	5 µL
Retention Time:	Ecamsule and Ecamsule-d_4: 0.8 minute
Run Time:	2.5 minutes

Mass Spectrometer conditions

Ionization Source and scan type:	Electro Spray Ionization (ESI); Multiple Reaction Monitoring (MRM)
Data acquisition:	Analyst 1.6.3

AB SCIEX 6500^{+} Q-TRAP mass spectrometer state file parameters:

Parameter	**Ecamsule**	**Ecamsule-d_4 (IS)**
Q1 mass/Q3 mass (amu)	563.3/481.2	567.3/485.2
Declustering potential, V	154	154
Collision Energy (V)	30	30
Collision Cell Exit Potential (V)	14	14
Source Temperature (^{0} C):	500	500
Ion Spray Voltage (V)	5000	5000
Collision Gas (CAD)	Medium	Medium
Curtain Gas (CUR)	30	30
Ion Source Gas 1 (GS1)	40	40
Ion Source Gas 2 (GS2)	50	50

Sample Preparation for Ecamsule: 100 µL of acetonitrile containing 6 ng/mL of Ecamsule–d_4 was added to MultiScreen® HV protein precipitation 96-well plates (0.45µm, Low Protein Binding, Hydrophilic) (Make: Merck, Part no MSHVN4550) and an aliquot of 30 µL of plasma sample was added to each well. The samples were

vortexed for 5 min, followed by centrifugation at 4000 rpm for 5 min. Then, 30µL of 10mM ammonium formate in 0.1% formic acid was added and shaken for 1 minute.

Validation Summary Table for Ecamsule

Description	**Ecamsule**
Short description of method	Protein precipitation with 96-well plates Reverse-phase HPLC with tandem mass spectrometric detection
Biological matrix	Human plasma (dipotassium ethylenediaminetetraacetic acid)
Analyte	Ecamsule
Internal standard (IS)	Ecamsule –d_4
Calibration concentrations	0.20 ng/mL to 10.00 ng/mL
QC concentrations	0.20 ng/mL, 0.60 ng/mL, 5.00 ng/mL, and 9.00 ng/mL
Selectivity	No significant interference observed in the 6 blank matrix lots screened.
Specificity	No significant interference observed.
Lower limit of quantitation	0.20 ng/mL Between-run accuracy 96% Between-run precision 19% Within-run accuracy 107% Within-run precision 18%
Between-run accuracy	93% to 97%
Between-run precision	3% to 10%
Within-run accuracy	97% to 103%
Within-run precision	2% to 8%
IS normalized matrix factor	LQC: 0.98 (%CV: 5) HQC: 1.00 (%CV: 2)
Dilution integrity	Concentration 30.00 ng/mL Diluted 5-fold: Accuracy 92%, Precision 6% Diluted 10-fold: Accuracy 93%, Precision 3%
Recovery of analyte	75% -84%
Recovery of IS	107%
Auto-sampler storage stability	Confirmed up to 24 hours at 5°C nominal. Accuracy 86% for LQC and 95% for HQC
Freeze thaw stability	Confirmed up to seven cycles, Accuracy 91% for LQC and 94% for HQC
Bench top stability	Confirmed up to 16 hours at 24°C nominal. Accuracy 95% for LQC and 91% for HQC
Stock solution stability	Confirmed up to 30 days at -20°C nominal. %Stability 105%
Injector Carryover	Not significant (not detected)
Co-administration drug effect	Accuracy LQC: 91% Accuracy HQC: 93%
Long term Stability in Plasma	Confirmed up to 125 days at -80°C nominal % Stability 107% for LQC and 87% for HQC
QC: Quality control; LQC: Low quality control; HQC: High quality control; CV: Coefficient of variance	

eTable 1. List of Active and Inactive Ingredients of the Sunscreen Products

Product	Active Ingredients	Inactive Ingredients
Spray #1	Avobenzone 3%, Homosalate 15%, Octisalate 5%, Octocrylene 2.35%, Oxybenzone 6%	Alcohol Denat., Isobutane, Dimethicone, Diethylhexyl 2,6 -Naphthalate, Trisiloxane, PPG-5-Ceteth-20, Acrylates/Octylacrylamide - Copolymer, Cyclopentasiloxane, Fragrance, Acrylates/Dimethicone Copolymer, Tocopheryl Acetate, Ascorbyl Palmitate, Retinyl Palmitate, Tocopherol
Spray #2	Avobenzone 3%, Octocrylene 10%, Oxybenzone 5%	Alcohol Denat., Isobutane, Isodecyl Neopentanoate, VA/butyl maleate/Isobornyl acrylate copolymer, Caprylyl Glycol, Menthyl Lactate, Mineral Oil, Aloe Barbadensis Leaf Extract, Fragrance
Lotion	Avobenzone 3%, Octocrylene 6%, Oxybenzone 4%	Water, Ethylhexyl Benzoate, Butyloctyl Salicylate, Cetearyl Alcohol, Diisopropyl Adipate, Phenethyl Benzoate, Phenoxyethanol, Polymethylsilsesquioxyane, VP/eicosene copolymer, Caprylyl Glycol, Dimethicone, Glycerine, Fragrance, Triethanolamine, Coco-Glucoside, Acrylates/C10-30 Alkyl acrylate crosspolymer, Methylparaben, Ceteth-10 Phosphate, Dicetyl Phosphate, Propylparaben, Disodium ethylenediaminetetraaceticacid, Paraffin, Xanthan Gum, Butyrospermum Parkii (Shea) butter, Mangifera Indica (Mango) seed butter, Sodium Ascorbyl Phosphate, Tocopheryl Acetate, Panthenol, Aloe Barbadensis Leaf Juice, Carica Papaya (Papaya) Fruit Extract, Colocasia Antiquorum Root Extract, Mangifera Indica (Mango) Fruit Extract, Passiflora Incarnata Fruit Extract, Plumeria Acutifolia Flower Extract, Psidium Guajava Fruit Extract
Cream	Avobenzone 2%, Ecamsule 2%, Octocrylene 10%	Carbomer 940, Carbomer Copolymer Type B, Cyclomethicone, Cimethicone, Edetate Disodium, Glycerin, Hydroxypropyl Methylcellulose, Isopropyl Palmitate, Methylparaben, Phenoxyethanol, Propylene Glycol, Propylparaben, Purified Water, Stearic Acid, Stearoyl Macrogolglycerides, Stearyl Alcohol, Trolamine

eTable 2. Demographics

Demographics		Population Total (N=24)	Spray#1 (N=6)	Spray#2 (N=6)	Lotion (N=6)	Cream (N=6)
Age, years (Mean ± SD)		35.5 ± 10.5	42.8 ± 13.0	33.7 ± 9.1	34.5 ± 6.9	31.7 ± 10.8
Race	Black or African American	14 (58.3 %)	1 (16.7 %)	4 (66.7 %)	4 (66.7 %)	5 (83.3 %)
	White	9 (37.5 %)	5 (83.3 %)	2 (33.3 %)	2 (33.3 %)	0 (0.0 %)
	Asian	1 (4.2%)	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	1 (16.7 %)
Ethnicity	Hispanic or Latino	4 (16.7 %)	2 (33.3 %)	0 (0.0 %)	1 (16.7 %)	1 (16.7 %)
	Not Hispanic or Latino	20 (83.3 %)	4 (66.7 %)	6 (100.0 %)	5 (83.3 %)	5 (83.3 %)
	Unknown	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)
Body mass index, kg/m2 (Mean ± SD)		25.0 ± 2.9	24.1 ± 3.2	24.0 ± 3.0	25.4 ± 2.5	26.7 ± 2.8
Weight, kg (Mean ± SD)		72.7 ± 12.4	70.9 ± 9.9	69.1 ± 12.5	73.2 ± 17.3	77.6 ± 10.4
Height, cm (Mean ± SD)		170.0 ± 10.1	171.7 ± 6.0	169.4 ± 9.4	168.4 ± 15.5	170.7 ± 9.9
Body surface area, m2 (Mean ± SD)		1.8 ± 0.2	1.8 ± 0.1	1.8 ± 0.2	1.8 ± 0.3	1.9 ± 0.2
Fitzpatrick skin type	I	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)
	II	1 (4.2%)	1 (16.7%)	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)
	III	5 (20.8%)	3 (50.0%)	1 (16.7%)	1 (16.7%)	0 (0.0 %)
	IV	4 (16.7%)	0 (0.0 %)	1 (16.7%)	3 (50.0%)	0 (0.0 %)
	V	8 (33.3%)	1 (16.7%)	2 (33.3%)	2 (33.3%)	3 (50.0%)
	VI	6 (25.0%)	1 (16.7%)	2 (33.3%)	0 (0.0 %)	3 (50.0%)

SD: Standard deviation

eTable 3. Complete Pharmacokinetic Parameters of Sunscreen Active Ingredients

Parameter	Spray#1 Geometric Mean [CV%] (range)	Spray#2 Geometric Mean [CV%] (range)	Lotion Geometric Mean [CV%] (range)	Cream Geometric Mean [CV%] (range)
Avobenzone				
C_{max} Overall (ng/mL)[a]	4.0 [60.9%] (1.6-8.3)	3.4 [77.3%] (1.0-7.3)	4.3 [46.1%] (2.8-9.3)	1.8 [32.1%] (1.1-2.7)
T_{max} Overall (h)[b]	77.0 (57.0-82.0)	67.5 (14.0-86.0)	67.5 (33.0-95.0)	69.0 (33.0-86.0)
C_{max} Day 1 (ng/mL)[a]	1.6 [43.0%] (1.0-3.0)	1.5 [92.9%] (0.4-4.4)	2.4 [69.4%] (1.0-5.2)	1.0 [43.8%] (0.5-1.6)
C_{max} Day 4 (ng/mL)[a]	3.8 [68.9%] (1.4-8.3)	3.1 [70.2%] (1.0-6.4)	3.5 [58.6%] (2.0-9.3)	1.7 [40.4%] (1.0-2.7)
T_{max} Day 1 (h)[b]	12.0 (8.0-23.0)	11.0 (6.0-23.0)	10.5 (6.0-23.0)	10.0 (9.0-23.0)
T_{max} Day 4 (h)[b]	79.5 (76.0-86.0)	80.0 (78.0-86.0)	82.5 (78.0-95.0)	82.0 (81.0-86.0)
AUC Day 1 (ng/mL*h)[c]	19.0 [42.5%] (11.4-28.3)	20.2 [84.4%] (5.3-43.6)	28.0 [60.9%] (12.3-56.6)	12.5 [40.3%] (6.1-17.5)
AUC Day 4 (ng/mL*h)[c]	52.8 [43.6%] (24.3-80.6)	45.8 [48.2%] (18.9-63.2)	56.2 [64.4%] (35.3-174.1)	30.1 [47.0%] (15.2-50.9)
Trough Day 2 (ng/mL)[d]	1.1 [46%] (0.5-1.7)	0.9 [99.1%] (0.2-2.0)	1.2 [105.1%] (0.5-5.2)	0.6 [74.0%] (0.2-1.1)
Trough Day 3 (ng/mL)[d]	1.7 [36.0%] (1.0-2.4)	1.4 [64.3%] (0.5-2.4)	1.8 [73.4%] (1.0-5.9)	1.0 [31.3%] (0.6-1.5)
Trough Day 4 (ng/mL)[d]	1.7 [61.6%] (0.6-3.2)	1.5 [58.6%] (0.6-3.0)	2.3 [78.7%] (1.2-8.0)	1.1 [75.6%] (0.5-2.6)
Residual Conc. Day 5 (ng/mL)[d]	1.8 [46.3%] (0.9-3.6)	1.6 [47.6%] (0.6-2.1)	2.2 [76.3%] (1.0-6.5)	1.0 [47.7%] (0.5-1.9)
Residual Conc. Day 6 (ng/mL)[d]	1.3 [66.9%] (0.5-2.7)	1.1 [38.3%] (0.7-1.9)	1.3 [68.0%] (0.8-3.5)	0.6 [82.2%] (0.3-1.2)
Residual Conc. Day 7 (ng/mL)[d]	0.9 [62.4%] (0.4-1.8)	0.7 [70.0%] (0.3-1.6)	1.2 [69.5%] (0.6-3.4)	0.3 [73.2%] (0.2-0.7)
Terminal Half Life (h)[e]	54.6 [57.0%] (29.8-114.0)	45.2 [68.0%] (27.6-128.1)	35.4 [13.4%] (31.3-40.8)	33.0 [48.0%] (22.4-68.4)
Oxybenzone				
C_{max} Overall (ng/mL)[a]	209.6 [66.8%] (83.3-532.0)	194.9 [52.4%] (89.3-350.1)	169.3 [44.5%] (103.3-274.6)	-
T_{max} Overall (h)[b]	57.0 (8.0-78.0)	32.5 (6.0-82.0)	21.5 (8.0-57.0)	-
C_{max} Day 1 (ng/mL)[a]	155.4 [56.4%] (70.9-271.1)	162.2 [81.8%] (46.1-350.1)	149.5 [38.4%] (97.0-270.2)	-
C_{max} Day 4 (ng/mL)[a]	177.6 [70.6%] (75.2-532.0)	163.0 [46.3%] (89.3-299.2)	118.1 [40.6%] (69.8-186.4)	-
T_{max} Day 1 (h)[b]	8.0 (4.0-12.0)	7.0 (6.0-12.0)	7.0 (4.0-10.0)	-
T_{max} Day 4 (h)[b]	78.0 (73.0-86.0)	80.0 (74.0-84.0)	74.0 (73.0-84.0)	-
AUC Day 1 (ng/mL*h)[c]	1948.2 [46.7%] (1128.3-3703.6)	1754.5 [80.5%] (515.8-3527.3)	1642.0 [21.9%] (1349.1-2349.6)	-
AUC Day 4 (ng/mL*h)[c]	2830.7 [48.2%] (1382.9-5424.5)	2317.7 [35.0%] (1290.0-3122.2)	1989.3 [32.7%] (1410.7-3101.0)	-

Parameter	Spray#1 Geometric Mean [CV%] (range)	Spray#2 Geometric Mean [CV%] (range)	Lotion Geometric Mean [CV%] (range)	Cream Geometric Mean [CV%] (range)
Trough Day 2 (ng/mL)[d]	57.8 [64.8%] (31.2-152.4)	51.2 [71.6%] (18.7-130.7)	53.2 [26.0%] (40.8-77.2)	-
Trough Day 3 (ng/mL)[d]	85.0 [44.7%] (46.1-137.6)	72.4 [57.4%] (31.8-161.6)	68.2 [34.2%] (49.7-117.6)	-
Trough Day 4 (ng/mL)[d]	77.1 [44.7%] (40.1-114.9)	68.9 [58.9%] (27.0-107.7)	69.7 [62.3%] (33.2-150.7)	-
Residual Conc. Day 5 (ng/mL)[d]	86.4 [56.5%] (38.5-145.8)	69.6 [27.6%] (48.0-102.3)	75.5 [38.9%] (40.0-102.6)	-
Residual Conc. Day 6 (ng/mL)[d]	46.0 [78.1%] (18.0-113.4)	32.7 [55.2%] (19.4-83.1)	28.3 [39.1%] (21.4-58.5)	-
Residual Conc. Day 7 (ng/mL)[d]	34.4 [51.4%] (15.6-56.1)	20.9 [52.0%] (9.8-42.4)	24.5 [78.0%] (14.0-86.8)	-
Terminal Half Life (h)[f]	30.6 [19.1%] (25.4-43.5)	23.5 [13.0%] (20.9-28.9)	27.1 [33.8%] (20.9-48.1)	-
Octocrylene				
C_{max} Overall (ng/mL)[a]	2.9 [102.0%] (1.0-9.8)	7.8 [113.3%] (2.5-20.4)	5.7 [66.3%] (2.8-13.4)	5.7 [47.1%] (2.9-10.3)
T_{max} Overall (h)[b]	74.5 (8.0-82.0)	65.0 (14.0-84.0)	54.5 (33.0-78.0)	72.0 (33.0-81.0)
C_{max} Day 1 (ng/mL)[a]	0.8 [53.0%] (0.5-1.7)	3.7 [125.7%] (1.1-18.5)	2.6 [65.6%] (1.2-6.3)	2.9 [39.9%] (1.6-4.2)
C_{max} Day 4 (ng/mL)[a]	2.6 [108.5%] (1.0-9.8)	6.2 [83.1%] (2.5-17.6)	3.9 [65.8%] (1.7-9.2)	4.9 [48.7%] (2.4-8.5)
T_{max} Day 1 (h)[b]	13.0 (8.0-23.0)	9.0 (6.0-14.0)	14.0 (8.0-23.0)	11.0 (8.0-23.0)
T_{max} Day 4 (h)[b]	78.5 (73.0-86.0)	78.0 (73.0-86.0)	79.5 (74.0-86.0)	81.0 (73.0-82.0)
AUC Day 1 (ng/mL*h)[c]	8.4 [43.5%] (4.4-14.1)	40.1 [90.7%] (14.1-136.8)	32.0 [64.6%] (16.7-84.0)	32.5 [28.9%] (19.4-45.3)
AUC Day 4 (ng/mL*h)[c]	28.0 [49.1%] (14.3-44.2)	84.0 [48.6%] (42.4-131.4)	60.9 [69.5%] (33.0-194.3)	69.5 [36.4%] (38.6-92.7)
Trough Day 2 (ng/mL)[d]	0.5 [43.7%] (0.4-0.9)	1.5 [67.6%] (0.7-3.3)	1.4 [108.6%] (0.6-6.3)	1.6 [73.5%] (0.6-4.2)
Trough Day 3 (ng/mL)[d]	0.8 [27.6%] (0.6-1.3)	2.6 [41.9%] (1.4-4.1)	2.0 [97.6%] (1.0-9.0)	2.3 [22.3%] (1.6-3.0)
Trough Day 4 (ng/mL)[d]	0.9 [36.3%] (0.6-1.3)	2.8 [59.4%] (1.3-6.2)	2.4 [83.7%] (1.1-9.8)	3.0 [94.6%] (1.5-10.3)
Residual Conc. Day 5 (ng/mL)[d]	0.9 [46.0%] (0.4-1.6)	2.6 [38.6%] (1.5-4.2)	2.3 [63.7%] (1.4-6.3)	2.1 [27.1%] (1.5-2.7)
Residual Conc. Day 6 (ng/mL)[d]	0.9 [74.1%] (0.4-2.6)	2.0 [40.7%] (1.3-3.4)	1.5 [81.9%] (0.6-4.2)	1.4 [52.3%] (0.9-3.1)
Residual Conc. Day 7 (ng/mL)[d]	0.6 [28.4%] (0.4-0.9)	1.2 [66.0%] (0.6-2.6)	1.7 [87.3%] (0.5-4.4)	1.3 [50.9%] (0.8-2.6)
Terminal Half Life (h)[g]	84.4 [52.2%] (59.3-120.2)	43.3 [50.7%] (26.9-75.2)	45.2 [27.9%] (36.9-55.6)	45.9 [27.9%] (33.9-62.8)
Ecamsule[h]				
C_{max} Overall (ng/mL)[a]	-	-	-	1.5 [166.1%] (0.5-12.1)
T_{max} Overall (h)[b]	-	-	-	28.0 (8.0-86.0)
C_{max} Day 1 (ng/mL)[a]	-	-	-	1.2 [177.3%] (0.4-12.1)

Parameter	Spray#1 Geometric Mean [CV%] (range)	Spray#2 Geometric Mean [CV%] (range)	Lotion Geometric Mean [CV%] (range)	Cream Geometric Mean [CV%] (range)
C_{max} Day 4 (ng/mL)[a]	-	-	-	0.7 [33.2%] (0.5-1.1)
T_{max} Day 1 (h)[b]	-	-	-	10.0 (8.0-23.0)
T_{max} Day 4 (h)[b]	-	-	-	81.0 (78.0-86.0)
AUC Day 1 (ng/mL*h)[c]	-	-	-	5.4 [488.3%] (0.4-90.1)
AUC Day 4 (ng/mL*h)[c]	-	-	-	3.8 [172.2%] (0.5-9.2)
Trough Day 2 (ng/mL)[d]	-	-	-	-
Trough Day 3 (ng/mL)[d]	-	-	-	-
Trough Day 4 (ng/mL)[d]	-	-	-	-
Residual Conc. Day 5 (ng/mL)[d]	-	-	-	-
Residual Conc. Day 6 (ng/mL)[d]	-	-	-	-
Residual Conc. Day 7 (ng/mL)[d]	-	-	-	-
Terminal Half Life (h)	-	-	-	-

C_{max}: Maximum concentration; T_{max}: Time at maximum concentration observed; AUC: Area under curve

[a]C_{max} is the maximum active ingredient concentration observed over the study duration. C_{max} Day 1 was the maximum concentration over the interval of 0 to 23 hr. C_{max} Day 4 was the maximum concentration over the interval of 71 to 95 hr.

[b]T_{max} is reported as median (range). T_{max} was the time of the maximum active ingredient concentration observed over the study duration. T_{max} Day 1 was the maximum concentration over the interval of 0 to 23 hr. T_{max} Day 4 was the maximum concentration over the interval of 71 to 95 hr.

[c]AUC Day 1 was calculated over the interval of 0 to 23 hr. AUC Day 4 was calculated over the interval of 71 to 95 hr.

[d]Trough Day 2, Trough Day 3, and Trough Day 4 samples were obtained at 23, 47, and 71 hr. Residual Concentration Day 5, Day 6, and Day 7 samples were obtained at 96, 120, and 144 hr.

[e]Terminal half-life for avobenzone is only reported for a subset of participants: spray #1 (n=5), spray #2 (n=5), lotion (n=3), and cream (n=5)

[f]Terminal half-life for oxybenzone is only reported for a subset of participants: spray #1 (n=6), spray #2 (n=5), and lotion (n=5)

[g]Terminal half-life for octocrylene is only reported for a subset of participants: spray #1 (n=2), spray #2 (n=4), lotion (n=3), and cream (n=4)

[h]Participant S4.2 had an ecamsule concentration of 12.1 ng/mL at 23 hr. Excluding this sample results in C_{max} Overall (ng/mL) of 1.2 [59.8%] (0.5-2.0), T_{max} Overall (h) of 20.2 (8-86), C_{max} Day 1 (ng/mL) of 0.8 [43.2%] (0.4-1.4), T_{max} Day 1 (h) of 9.4 [15.7%] (8-12), and AUC Day 1 (ng/mL*h) of 2.1

eTable 4. Incidence and Number of Adverse Events by Treatment Group

Adverse Event	Spray#1 Incidence (number of events)	Spray#2 Incidence (number of events)	Lotion Incidence (number of events)	Cream Incidence (number of events)
Abdominal Pain	0	0	1 (1)	0
Chapped lips	0	1 (1)	0	1 (1)
Diarrhea	0	0	1 (1)	0
Dizziness	0	0	1 (1)	0
Eye burning	0	0	0	1 (1)
Eye irritation	0	0	1 (1)	0
Fatigue	0	0	1 (1)	0
Headache	0	0	1 (2)	0
Lip swelling	0	0	0	1 (1)
Milia	0	0	0	1 (4)
Neck pain	0	0	0	1 (1)
Paresthesia	0	0	0	1 (1)
Pruritus	0	0	1 (4)	1 (1)
Rash	1 (1)	1 (2)	1 (1)	1 (1)

First number stands for incidence and second number in parenthesis stands for number of events.
There were 6 subjects per treatment group.
This table reports all Medical Dictionary for Regulatory Activities (MedDRA v.21.1)-defined adverse events during the study.

eTable 5. Comparison of Day 4 With Day 1 Values of AUC and C_{max} of Sunscreen Active Ingredients

Parameter[a,b]	Spray#1 Geometric Mean [CV%] (range)	Spray#2 Geometric Mean [CV%] (range)	Lotion Geometric Mean [CV%] (range)	Cream Geometric Mean [CV%] (range)
Avobenzone				
C_{max} Day 1 (ng/mL)	1.6 [43.0%] (1.0-3.0)	1.5 [92.9%] (0.4-4.4)	2.4 [69.4%] (1.0-5.2)	1.0 [43.8%] (0.5-1.6)
C_{max} Day 4 (ng/mL)	3.8 [68.9%] (1.4-8.3)	3.1 [70.2%] (1.0-6.4)	3.5 [58.6%] (2.0-9.3)	1.7 [40.4%] (1.0-2.7)
GMR (90% CI) Day 4 vs Day 1	2.38 (1.68; 3.37)	2.02 (1.27; 3.21)	1.47 (1.05; 2.05)	1.75 (1.27; 2.40)
AUC Day 1 (ng/mL*h)	19.0 [42.5%] (11.4-28.3)	20.2 [84.4%] (5.3-43.6)	28.0 [60.9%] (12.3-56.6)	12.5 [40.3%] (6.1-17.5)
AUC Day 4 (ng/mL*h)	52.8 [43.6%] (24.3-80.6)	45.8 [48.2%] (18.9-63.2)	56.2 [64.4%] (35.3-174.1)	30.1 [47.0%] (15.2-50.9)
GMR (90% CI) Day 4 vs Day 1	2.77 (2.28; 3.38)	2.27 (1.69; 3.03)	2.00 (1.44; 2.79)	2.46 (2.01; 3.01)
Oxybenzone				
C_{max} Day 1 (ng/mL)	155.4 [56.4%] (70.9-271.1)	162.2 [81.8%] (46.1-350.1)	149.5 [38.4%] (97.0-270.2)	-
C_{max} Day 4 (ng/mL)	177.6 [70.6%] (75.2-532.0)	163.0 [46.3%] (89.3-299.2)	118.1 [40.6%] (69.8-186.4)	-
GMR (90% CI) Day 4 vs Day 1	1.14 (0.82; 1.59)	1.00 (0.75; 1.34)	0.79 (0.55; 1.14)	
AUC Day 1 (ng/mL*h)	1948.2 [46.7%] (1128.3-3703.6)	1754.5 [80.5%] (515.8-3527.3)	1642.0 [21.9%] (1349.1-2349.6)	-
AUC Day 4 (ng/mL*h)	2830.7 [48.2%] (1382.9-5424.5)	2317.7 [35.0%] (1290.0-3122.2)	1989.3 [32.7%] (1410.7-3101.0)	-
GMR (90% CI) Day 4 vs Day 1	1.45 (1.17; 1.80)	1.32 (0.93; 1.86)	1.21 (1.00; 1.46)	
Octocrylene				
C_{max} Day 1 (ng/mL)	0.8 [53.0%] (0.5-1.7)	3.7 [125.7%] (1.1-18.5)	2.6 [65.6%] (1.2-6.3)	2.9 [39.9%] (1.6-4.2)
C_{max} Day 4 (ng/mL)	2.6 [108.5%] (1.0-9.8)	6.2 [83.1%] (2.5-17.6)	3.9 [65.8%] (1.7-9.2)	4.9 [48.7%] (2.4-8.5)
GMR (90% CI) Day 4 vs Day 1	3.12 (1.52; 6.38)	1.69 (0.75; 3.84)	1.53 (0.95; 2.45)	1.78 (1.38; 2.30)
AUC Day 1 (ng/mL*h)	8.4 [43.5%] (4.4-14.1)	40.1 [90.7%] (14.1-136.8)	32.0 [64.6%] (16.7-84.0)	32.5 [28.9%] (19.4-45.3)
AUC Day 4 (ng/mL*h)	28.0 [49.1%] (14.3-44.2)	84.0 [48.6%] (42.4-131.4)	60.9 [69.5%] (33.0-194.3)	69.5 [36.4%] (38.6-92.7)
GMR (90% CI) Day 4 vs Day 1	3.33 (2.37; 4.68)	2.09 (1.41; 3.11)	1.90 (1.59; 2.27)	2.15 (1.87; 2.48)

Parameter[a,b]	Spray#1 Geometric Mean [CV%] (range)	Spray#2 Geometric Mean [CV%] (range)	Lotion Geometric Mean [CV%] (range)	Cream Geometric Mean [CV%] (range)
Ecamsule				
C_{max} Day 1 (ng/mL)	-	-	-	1.2 [177.3%] (0.4-12.1)
C_{max} Day 4 (ng/mL)	-	-	-	0.7 [33.2%] (0.5-1.1)
GMR (90% CI) Day 4 vs Day 1				0.53 (0.16; 1.70)
AUC Day 1 (ng/mL*h)	-	-	-	5.4 [488.3%] (0.4-90.1)
AUC Day 4 (ng/mL*h)	-	-	-	3.8 [172.2%] (0.5-9.2)
GMR (90% CI) Day 4 vs Day 1				0.76 (0.21; 2.78)

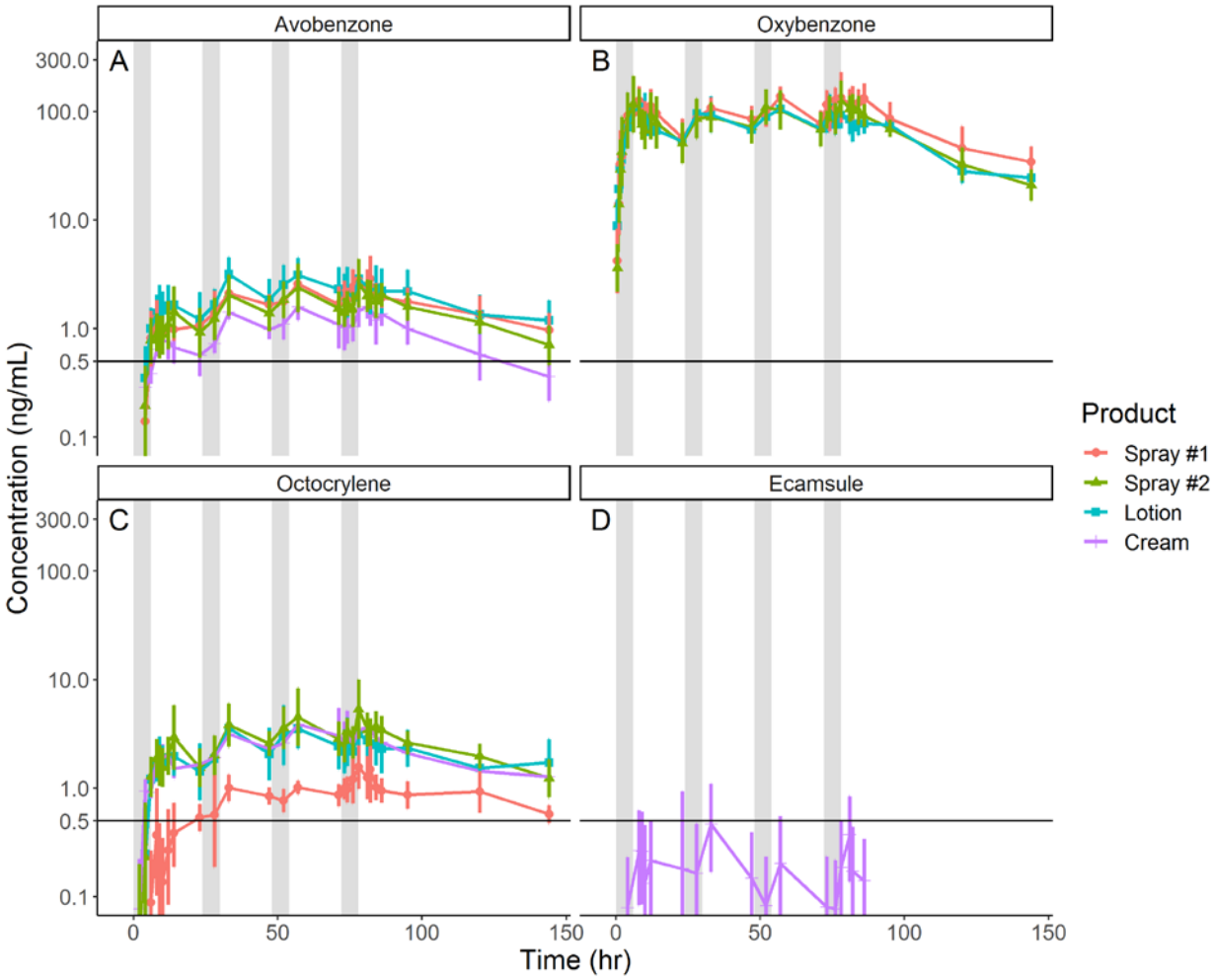
C_{max}: Maximum concentration; AUC: Area under curve; GMR: Geometric mean ratio

[a]C_{max} Day 1 was the maximum concentration over the interval of 0 to 23 hr. C_{max} Day 4 was the maximum concentration over the interval of 71 to 95 hr.

[b]AUC Day 1 was calculated over the interval of 0 to 23 hr. AUC Day 4 was calculated over the interval of 71 to 95 hr.

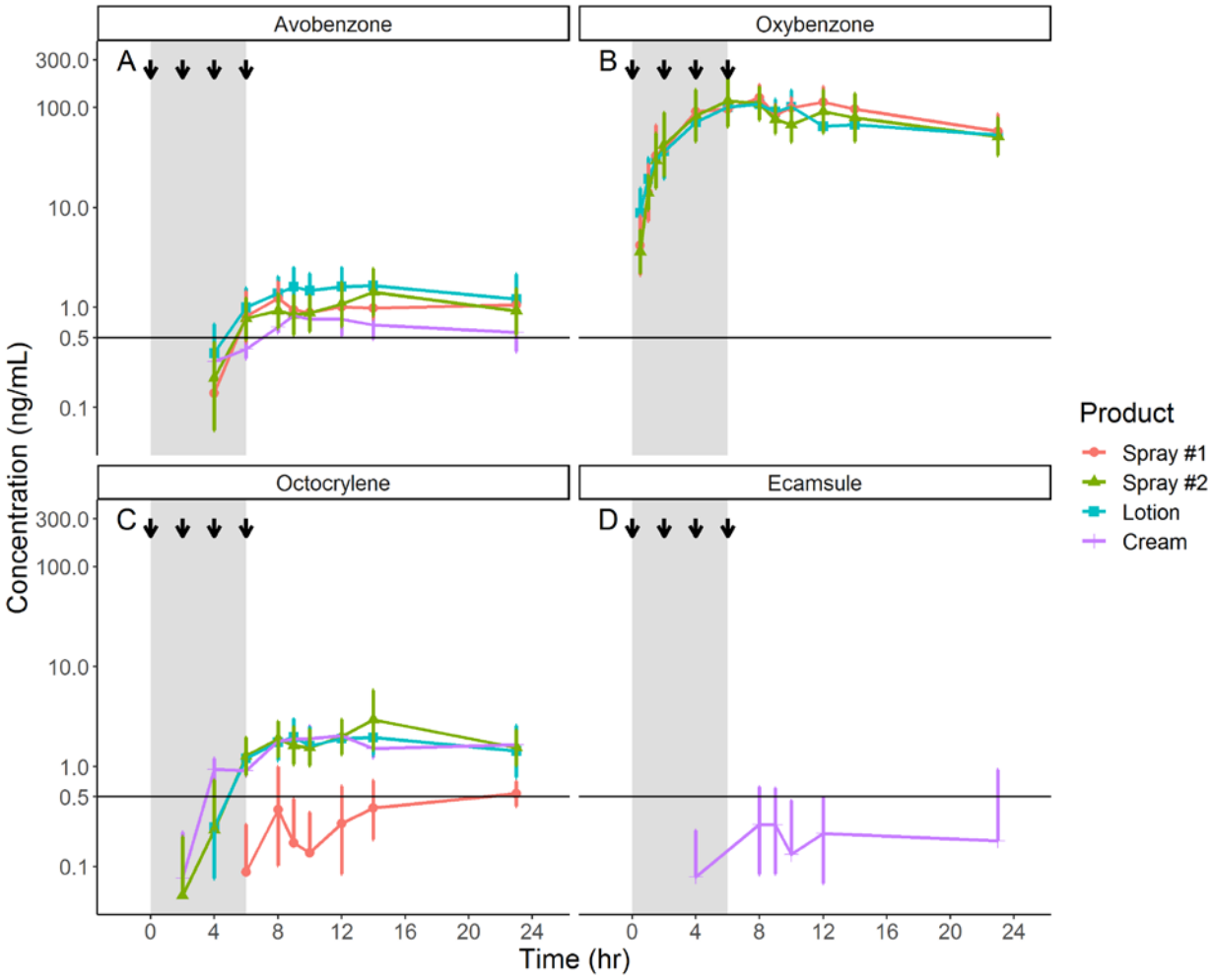
eFigure 1. Geometric Mean Concentration Profiles (All Data)

Pharmacokinetic profiles of (A) avobenzone, (B) oxybenzone, (C) octocrylene and (D) ecamsule. Horizontal lines on the graphs represent 0.5 ng/mL. Products are listed on the graphs. Each point and corresponding vertical line represent the geometric mean and 90% confidence interval of 6 participants, except for the cream product (n=6 but one participant discontinued after day 2). The gray vertical shaded regions indicate the 6-hour window (e.g., at 0, 2, 4 and 6 hours) of sunscreen application.



eFigure 2. Geometric Mean Concentration Profiles (Day 1)

Pharmacokinetic profiles of (A) avobenzone, (B) oxybenzone, (C) octocrylene and (D) ecamsule on day 1 only. Horizontal lines on the graphs represent 0.5 ng/mL. Products are listed on the graphs. Each point and corresponding vertical line represent the geometric mean and 90% confidence interval of 6 participants, except for the cream product (n=6 but one participant discontinued after day 2). The gray vertical shaded regions indicate the 6-hour window (e.g., dosing denoted with arrows at 0, 2, 4 and 6 hours) of sunscreen application.



eDictionary. Data Dictionary for Participant Data Listings

A full listing of participant data, including demographics and concentration by product and analyte at each time point are included with this study. Column names and definitions are provided below:

Variable	Definition
Participant	Participant ID
Product	Administered product. One of Spray #1, Spray #2, Lotion, or Cream
Analyte	Measured analyte. One of Avobenzone, Oxybenzone, Octocrylene, or Ecamsule
Time	Nominal sampling time (unit = hours)
Concentration	Reported concentration with BLQ values set to zero. (unit = ng/mL)
BLQ	Denotes samples below the limit of quantitation. Limits were 0.2 ng/mL for Avobenzone, 0.4 ng/mL for Oxybenzone, 0.4 ng/mL for Octocrylene, and 0.2 ng/mL for Ecamsule
Age	Age of the participant (unit = years)
Gender	Gender of the participant (one of 'Female' or 'Male')
Ethnicity	Ethnicity of the participant (one of 'Hispanic or Latino' or 'Not Hispanic or Latino')
Race	Race of the participant (one of 'Asian', 'Black or African American', or 'White')
Height	Height of the participant (unit = cm)
Weight	Weight of the participant (unit = kg)
BMI	Body mass index of the participant (unit = kg/m^2)
BSA	Body surface area of the participant (unit = m^2)
Fitzpatrick Skin Type	Fitzpatrick Skin Type (one of I, II, III, IV, V, or VI)

eReferences

1. Janjua NR, Mogensen B, Andersson AM et al. Systemic absorption of the sunscreens benzophenone-3, octyl-methoxycinnamate, and 3-(4-methyl-benzylidene) camphor after whole-body topical application and reproductive hormone levels in humans. *J Invest Dermatol*. 2004; 123(1):57–61.