A 4 Day, Randomized Study to Evaluate the Potential of MC2-01 Cream to Induce a Phototoxicity Skin Reaction in Healthy Subjects, Using a Controlled Photopatch Test Design

Statistical Analysis Plan

Sponsor Protocol No. MC2-01-C9
TKL Study No. PB610818

18 February 2019

Johan Selmer, MD
Chief Medical Officer
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1. STUDY PROTOCOL AND AMENDMENTS

This Statistical Analysis Plan is based on the protocol version Amendment 1 dated 10 January 2019.

2. OBJECTIVES

The primary objective of this study will be to determine the phototoxic potential of MC2-01 when topical application to healthy skin is followed by light exposure.

In addition, safety will be assessed by evaluation of any AEs reported during the study.

3. STUDY DESIGN

This will be a single-center, randomized, double-blind, controlled, within-subject comparison study of the investigational products (IPs), MC2-01 Cream and MC2-01 Vehicle in healthy volunteer subjects. MC2-01 Cream and MC2-01 Vehicle will each be applied to 2 sites, one which will be irradiated and one which will remain non-irradiated. The irradiated and nonirradiated sites will be compared with each other and with an untreated irradiated site.

A total of 4 application sites (2 cm x 2 cm each) will be marked on the subject's infrascapular region of the back: 2 sites for MC2-01 Cream and 2 sites for MC2-01 Vehicle. Each study product will be applied according to the randomization scheme in an amount of 0.2 g under semi-occlusive patch conditions once during the study.

Approximately 24 (±2) hours post study product application, the patches will be removed by study staff. The sites will then be graded for cutaneous reactions by a trained evaluator and the designated sites, including the untreated site, will be exposed to irradiation. One set (MC2-01

Cream and MC2-01 Vehicle patches) on the back will be designated for irradiation and the other set will remain non-irradiated. An additional site on the back will be marked which will receive no treatment but will receive irradiation to serve as an untreated irradiated control. The sites will be examined at approximately 24 and 48 hours post irradiation and graded for reactions.

Cutaneous reactions at the application sites will be evaluated using a visual scale that rates the degree of erythema, edema, and other signs of cutaneous irritation (see Table 1).

Safety evaluations include collection of AEs.

4. DATA SETS

The study database will be constructed and maintained by TKL Data Management in accordance with its standard operating procedures (SOPs) and the Sponsor's specifications. A data management plan (DMP), including database/screen design specifications, CRF review guidelines, coding instructions, and edit check specifications will be submitted to the Sponsor for review prior to data

entry. When the database has been declared to be complete and accurate as per the DMP, the database will be locked (i.e., the database software will not allow any further additions to, removals from, or other edits of the database). All changes to the database after that time must be authorized by the Sponsor in writing and a database unlock form and then the re-lock form will be signed by both TKL and Sponsor. Study Data Tabulation Model (SDTM) datasets will be constructed from the raw data sets. Analysis datasets (ADaM) that are necessary for table analyses will be generated from SDTM.

The study SDTM and ADaM datasets will be taken as input to validated SAS programs which generate the report-ready tables and listings. Each output display will show the names of the data sets and SAS program used to produce it. Upon completion of the study report, the data sets will be provided to the sponsor as SAS XPT transport files. Data sets will be CDISC compliant. A CDISC compliant define.xml and annotated CRF for SDTM datasets will also be provided to the sponsor.

5. HARDWARE AND SOFTWARE

Statistical analysis will be performed following TKL SOP 03-02-04 Preparation of Tables and Listings for Statistical Reporting. All statistical analysis will be performed using SAS Version 9.2 or higher with program code prepared specifically for the project by qualified TKL statisticians and SAS programmers.

The SAS programs will generate rich-text-formatted (RTF) output with the "RTF" extension using the SAS Output Delivery System (ODS). The summary tables and listings will be formatted using the Courier New 9-point font. The RTF output is included in report documents prepared with Microsoft Word and converted to PDF format without typographical change.

6. CODING

The Medical Dictionary for Regulatory Activities (MedDRA, Version 22.0 2019) coding dictionary will be used for the assignment of system organ class and preferred terms to AEs. The WHO Drug Dictionary Enhanced (WHO DDE Version B 1Q19) will be used for assignment of preferred terms and drug classifications (i.e., Anatomic-Therapeutic-Chemical [ATC] subgroups) to concomitant medications, as described in the Data Management Plan (DMP).

7. STATISTICAL DATA REVIEW

Data verification activities to be performed prior to delivery of the SAS datasets to the project statistician are described in the approved DMP. After completion of the data verification activities, the SAS datasets will be delivered to the project statistician along with documentation of any unresolved queries and data conventions applied that are not fully explained in the data or the DMP. After delivery of the SAS datasets and prior to unblinding of the study data, the project statistician will perform completeness and self-consistency checks of the study data. Queries will be issued to the Data Manager and resolved before closure of the database.

8. HANDLING OF MISSING DATA

Missing values will not be imputed. In the tables and listings, percentages are rounded to the nearest tenth and p-values are rounded to the nearest thousandth.

9. DATABASE CLOSURE

After completion of all data review procedures, validation of the project database, and approval of the final database in writing by the Sponsor, the database will be closed ("locked"). After the closure of the clinical database and authorization to unblind the study, the treatment codes will be merged to the analysis data sets. Any changes to data, coding, populations, or analysis plan after database closure must be approved by the Sponsor, in writing, and TKL management, and documented in the study archive with a detailed explanation of changes and reasons for changes.

10.INTERIM AND SUBGROUP ANALYSES

No interim or subgroup analyses are planned.

11.STATISTICAL EVALUATION

11.1 General Considerations for Data Analyses

The focus of the statistical analysis will be the comparison with controls of the phototoxic response to the study products. The parameter for phototoxicity will be the mean of Day 3 and 4 scores (sum of erythema and edema).
All statistical processing will be performed using the SAS® system (version 9.2).

11.2 Analysis Populations

All subjects who receive treatment will be evaluable for safety (adverse events). The evaluation of phototoxicity potential of the study products will be assessed for all subjects completing the study.

11.3 Subject Disposition

The number of subjects screened, randomized, completed, and discontinued (by reason for discontinuation) will be summarized using descriptive statistics.

11.4 Background and Demographic Characteristics

Descriptive statistics will be used to summarize demographic characteristics (i.e., age, gender, ethnicity, and race) and background characteristics (i.e. Fitzpatrick skin type and MED) for the randomized subject population. Past/coexistent medical history information for all randomized

subjects will be presented in a by-subject listing. Urine pregnancy test results will be presented in a by-subject listing.

11.5 Study Products/Visit Compliance

Descriptive statistics will be used to summarize study product compliance for the randomized subject population.

11.6 Prior and Concomitant Medications

Prior and concomitant medication information for all randomized subjects will be presented in a by-subject listing.

11.7 Dermal Response Evaluation

The following response symbols, numerical equivalents and notations will be used for the evaluation of dermal response at each application and control site on Days 2 through 4.

Table 1: Grading of Responses

Response	Symbol	Numerical Equivalent Score
Erythema		
No reaction	-	0
Mild, but definite erythema	+	1
Moderate erythema	++	2
Marked/severe erythema	+++	3
Edema		
No Reaction	-	0
Mild, but definite edema	**	1
Definite edema with erosion/vesiculation	***	2

Table 2: Response Notations

Response/Comment	Notation
Hyperpigmentation	Hr
Hypopigmentation	Ho
Vesiculation	V
Papular response	p
Papulovesicular response	pv
Damage to epidermis: oozing, crusting, and/or superficial erosions	D
Itching	I
Spreading of reaction beyond patch study site (i.e., reaction where material did not contact skin)	S
Follicular irritation with or without pustule formation (folliculitis)	f
Subject absent	X
Patch dislodged	PD
Not patched	NP
No Reaction	0

All assigned scores for subjects who complete the study will be summarized using frequency counts by treatment for Days 2, 3 and 4.

Response scores are defined as the sum of the erythema and edema scores at each time point (Days 2, 3 and 4).

Selected pairwise comparisons will be performed on the mean of the Day 3 and Day 4 response scores in the context of the 2-way analyses of variance (ANOVA), including main effects of subject and treatment, without interaction. Pairs to be compared are: each study product irradiated versus non-irradiated and all pairwise comparisons of each set (MC2-01 Cream versus MC2-01 Vehicle on both the irradiated and non-irradiated sides, MC2-01 Cream versus untreated on the irradiated side, and MC2-01 Vehicle versus untreated on the irradiated side).

In case of gross violations of the model assumptions (normality, homoscedasticity), non-parametric analysis will be performed. The irritation scores for each treatment will be ranked within subject and compared pairwise using Wilcoxon signed-rank test.

11.8 Adverse Events

Adverse events will be coded for this study, as specified in the DMP. Adverse events will be summarized as an overall incidence of at least one event, incidence within body systems only, incidence by body system and preferred term, and by highest severity. Each subject will contribute only once (e.g., the first occurrence) to each of the rates, regardless of the number of occurrences (events) the subject experiences.

Treatment-emergent AEs will be summarized and tabulated by the system organ class and preferred term, by severity (mild, moderate, severe) and by relationship to study product (not related, possibly related, probably related, and definitely related). Treatment-emergent will be defined as any AE with an onset date on or after the first study product administration date. Any event with a missing onset date will be included as a treatment-emergent AE. Serious adverse events and deaths will be listed by subject.

11.9 Rationale for Selection of Sample Size

The sample size of 30 evaluable subjects conforms to industry and regulatory standards for determination of irritation when topical application to skin is followed by light exposure.

12.CHANGES FROM THE PROTOCOL AND PLANNED ANALYSES

There are no changes from the analysis plan specified in the protocol.

13.HEADINGS

Each page of the analysis will show the Sponsor's name and study number. Report tables will be embedded in the Microsoft Word report document from SAS program output without change. The header of each table and listing will include the page number as "Page X of Y," with Y being the total number of pages for that table or listing and X being the specific page number. The footer of each table will show the name of the SAS program module which generated it, the names of all datasets providing input data in the program and the date and time the table was generated.

14.ARCHIVING

After finalization of the analysis, the following will be archived at TKL Research, Inc. and/or with the Sponsor:

- Randomization list
- Statistical Analysis Plan
- Data Management Plan
- Annotated CRF
- All SAS code used in the project for statistical analysis
- Final delivered tables and listings as included in the clinical study report
- Final SAS datasets, with full audit trail from initial data entry through final accepted version
- ADaM datasets that are necessary for analysis will be programmed in addition to SDTM
- Define.xml

- Study data and analysis data reviewer guides for any unavoidable CDISC-checker errors or warnings
- Relevant Correspondence

15.OUTLINE OF PROPOSED TABLES, LISTINGS AND FIGURES

Summary Tables

Table Number	Title
14.1.1	Summary of Subject Enrollment and Disposition
14.1.2	Summary of Subject Demographics and Baseline Characteristics
14.1.3	Summary of Study Product and Visit Compliance
14.2.1.1	Summary of Dermal Responses by Response Scores and Notations
14.2.1.2	Summary of Dermal Responses by Response Scores
14.3.1.1	Overall Summary of Adverse Events
14.3.1.2	Summary of Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Maximum Relationship to Study Product*
14.3.1.3	Summary of Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Maximum Severity*

*Tables 14.3.1.2 and 14.3.1.3 will only be included if there are a sufficient number of AEs for multiple classified AE tables.

Data Listings

Listing Number	Title
16.1.7	Subject Randomization
16.2.1	Subject Disposition and Population Inclusion
16.2.2	Protocol Deviations
16.2.4.1	Demographics and Baseline Characteristics
16.2.4.2	Medical History
16.2.4.3	Prior and Concomitant Medications
16.2.5	MED Determination
16.2.6	Assessment of Dermal Responses
16.2.7.1	Adverse Events
16.2.7.2	Serious Adverse Events and Deaths
16.2.8	Urine Pregnancy Test Results
16.2.9	Comments

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Table 14.1.1: Summary of Subject Enrollment and Disposition

Number of Subjects Screened	XX
Screen Failures, n (%) [1]	XX (XX.X)
Reason Not Randomized, n (%)	
Inclusion X: XXXXXXXXXXXXXXXXXXXXXXX	XX (XX.X)
Exclusion X: XXXXXXXXXXXXXXXXXXXXXXX	XX (XX.X)
Other	XX (XX.X)
Etc.	
Number of Subjects Randomized	XX
Number of Subjects Completing Study, n (%)	XX (XX.X)
Subjects Included in Analysis of Phototoxicity (Population I), n (%)	XXX (XX.X)
Subjects Included in Analysis of Adverse Events (Population II), n (%)	XXX (XX.X)
Number of Subjects Discontinued, n (%)	XX (XX.X)
Reason for Discontinuation, n (%)	
Protocol Violation	X (XX.X)
Withdrawal of informed consent	X (XX.X)
Etc.	

Note: Percentages are relative to the number of randomized subjects except where otherwise specified.

[1] Percentage is relative to total number screened.

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Table 14.1.2: Summary of Subject Demographics and Baseline Characteristics
All Randomized Subjects

		(N=XX)
Age (years)	Mean (SD)	XX.XX (X.XX)
	Median	XX.X
	Minimum, Maximum	XX.X, XX.X
Gender, n (%)	Male	XX (XX.X)
	Female	XX (XX.X)
Race, n (%)	White	XX (XX.X)
	Black or African American	XX (XX.X)
	Asian	XX (XX.X)
	American Indian or Alaskan Native	XX (XX.X)
	Native Hawaiian or Other Pacific Islander	XX (XX.X)
	Other	XX (XX.X)
Ethnicity, n (%)	Hispanic or Latino	XX (XX.X)
	Not Hispanic or Latino	XX (XX.X)
Fitzpatrick Skin Type, n (%) [1]	I	XX (XX.X)
	II	XX (XX.X)
	III	XX (XX.X)
MED	Mean (SD)	X.XX (X.XX)
	Minimum, Maximum	X.XX, X.XX

[1] I = Always burns easily, never tans; II = Always burns easily, tans minimally; III = Burns moderately, tans gradually

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Table 14.1.3: Summary of Study Product and Visit Compliance
All Randomized Subjects

	Number of Subjects Attending, n(%) [1]	**Number of Subjects with Study Product Applied, Removed, Irradiated, and Evaluated, n (%) [2]**		
		MC2-01 Cream	**MC2-01 Vehicle**	**Untreated**
Day1 Screening/Randomization	XX (XX.XX)	xx (XX.XX)	xx (XX.XX)	xx (XX.XX)
Day 2	XX (XX.XX)	xx (XX.XX)	xx (XX.XX)	xx (XX.XX)
Day 3	XX (XX.XX)	xx (XX.XX)	xx (XX.XX)	xx (XX.XX)
Day 4/ End of Study	XX (XX.XX)	xx (XX.XX)	xx (XX.XX)	xx (XX.XX)

[1] The denominator of total number of randomized subjects is used to calculate the percentages.
[2] The denominator of total number of subjects attending each visit is used to calculate the percentages.

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Table 14.2.1.1: Summary of Dermal Responses by Response Scores and Notations
All Randomized Subjects

	MC2-01 Cream		MC2-01 Vehicle		Untreated
Response [1]	**Irradiated**	**Non-Irradiated**	**Irradiated**	**Non-Irradiated**	**Irradiated**
0 hours (Day 2), n (%)					
0	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
1Hr	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
etc.	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
24 hours (Day 3), n (%)					
0	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
etc.	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
48 hours (Day 4), n (%)					
0	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
etc.	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

[1] Response score is the sum of erythema and edema.

Scores:
Erythema: 0 = No reaction; 1 = Mild, but definite erythema; 2 = Moderate erythema; 3 = Marked/severe erythema;
Edema: 0 = No reaction; 1 = Mild, but definite edema; 2 = Definite edema with erosion/vesiculation

Notations:
Hr = hyperpigmentation; Ho = hypopigmentation; V = vesiculation; p= Papular response; pv= Papulovesicular response; D= Damage to epidermis; oozing, crusting, and/or superficial erosions; I=Itching; S= Spreading of reaction beyond patch study site (i.e., reaction where material did not contact skin); f= Follicular irritation with or without pustule formation (folliculitis).; X=Subject absent; PD=Patch dislodged; NP = Not Patched ; 0=No Reaction

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Table 14.2.1.1: Summary of Dermal Responses by Response Scores and Notations
All Randomized Subjects

	MC2-01 Cream		**MC2-01 Vehicle**		**Untreated**
Response	**Irradiated**	**Non-Irradiated**	**Irradiated**	**Non-Irradiated**	**Irradiated**
Average of 24 & 48 hrs					
N	xx	xx	xx	xx	xx
Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
P values					
vs MC2-01 Cream, Irradiated	--	x.xxx	x.xxx	x.xxx	x.xxx
vs MC2-01 Cream, Non-irradiated		--	x.xxx	x.xxx	x.xxx
vs MC2-01 Vehicle, Irradiated			--	x.xxx	x.xxx
vs MC2-01 Vehicle, Non-irradiated				--	x.xxx
vs Untreated, Irradiated					--

Note: P values are from an analysis of variance of the average numerical score (sum of erythema and edema) at 24 and 48 hours (Days 3 and 4), with effects of subject and treatment, using Fisher's least significant differences.

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Table 14.2.1.2: Summary of Dermal Responses by Response Scores
All Randomized Subjects

	MC2-01 Cream		MC2-01 Vehicle		Untreated
Response [1]	**Irradiated**	**Non-Irradiated**	**Irradiated**	**Non-Irradiated**	**Irradiated**
0 hours (Day 2), n (%)					
0	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
etc.	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
24 hours (Day 3), n (%)					
0	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
etc.	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
48 hours (Day 4), n (%)					
0	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
etc.	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

[1] Response score is the sum of erythema and edema.

Scores:
Erythema: 0 = No reaction; 1 = Mild, but definite erythema; 2 = Moderate erythema; 3 = Marked/severe erythema;
Edema: 0 = No reaction; 1 = Mild, but definite edema; 2 = Definite edema with erosion/vesiculation

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Table 14.2.1.2: Summary of Dermal Responses by Response Scores
All Randomized Subjects

	MC2-01 Cream		MC2-01 Vehicle		Untreated
Response	**Irradiated**	**Non-Irradiated**	**Irradiated**	**Non-Irradiated**	**Irradiated**
Average of 24 & 48 hrs					
N	xx	xx	xx	xx	xx
Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
P values					
vs MC2-01 Cream, Irr	--	x.xxx	x.xxx	x.xxx	x.xxx
vs MC2-01 Cream, Non-irr		--	x.xxx	x.xxx	x.xxx
vs MC2-01 Vehicle, Irr			--	x.xxx	x.xxx
vs MC2-01 Vehicle, Non-irr				--	x.xxx
vs Untreated, Irr					--

Note: P values are from an analysis of variance of the average numerical score (sum of erythema and edema) at 24 and 48 hours (Days 3 and 4), with effects of subject and treatment, using Fisher's least significant differences.

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Table 14.3.1.1: Overall Summary of Adverse Events
Safety Population

	Safety Population (N = XX)
Subjects with Any AE, n (%)	XX (XX.X)
Event Number of AEs	XX
Subjects with Any Treatment-emergent AE (TEAE), n (%) [1]	XX (XX.X)
Event Number of Treatment-emergent AEs	XX
Subjects with Any Treatment-related TEAE, n (%) [2]	XX (XX.X)
Event Number of Treatment-related TEAEs	XX
Subjects with Any Serious TEAE, n (%)	XX (XX.X)
Event Number of Serious TEAEs	XX
Subjects with Any Severe TEAE, n (%)	XX (XX.X)
Event Number of Severe TEAEs	XX
Subjects with Any Moderate TEAE, n (%)	XX (XX.X)
Event Number of Moderate TEAEs	XX
Subjects with Any Mild TEAE, n (%)	XX (XX.X)
Event Number of Mild TEAEs	XX
Subjects with Any TEAE Leading to Discontinuation of Study Medication, n (%)	XX (XX.X)
Event Number of TEAEs Leading to Discontinuation of Study Medication	XX
<< **Adverse Event System Organ Class**>>	XXX (XX.X)
<<Adverse Event Preferred Term>>	XXX (XX.X)
<<Adverse Event Preferred Term>>	XXX (XX.X)
<Programming note: sort by number of subjects so that the AE System Organ Classes and Preferred Terms with the highest frequencies appear first>	

[1] A treatment-emergent AE is an AE with an onset date on or after the first study product administration date.
[2] Treatment-related TEAEs include definitely related, probably related, and possibly related.

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Table 14.3.1.2: Summary of Treatment-Emergent Adverse Events
by System Organ Class, Preferred Term, and Maximum Relationship to Study Product
Safety Population

	(N = XX)				
	Total N (%)	**Definitely N (%)**	**Probably N (%)**	**Possibly N (%)**	**Not Related N (%)**
Subjects with Any Treatment-Emergent AE	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Total Number of Treatment-Emergent AEs	XX	XX	XX	XX	XX
<< Adverse Event System Organ Class>>	XXX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
<<Adverse Event Preferred Term>>	XXX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
<<Adverse Event Preferred Term>>	XXX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
<Programming note: sort by number of subjects so that the AE System Organ Classes and Preferred Terms with the highest frequencies appear first>					

Note: Table entries are number (%) of subjects.

Treatment-emergent AE is defined as any AE with an onset date on or after the first study product administration date (or with onset before dosing and worsening after dosing). Counts reflect numbers of subjects reporting one or more adverse events that map to the MedDRA (version 22.0) system organ class or preferred term. A subject may be counted once only in each row at the most related rating.

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Table 14.3.1.3: Summary of Treatment-Emergent Adverse Events
by System Organ Class, Preferred Term and Maximum Severity
Safety Population

	(N = XX)			
	Total	**Mild**	**Moderate**	**Severe**
	N (%)	**N (%)**	**N (%)**	**N (%)**
Subjects with Any Treatment-Emergent AE	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Total Number of Treatment-Emergent AEs	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
<< Adverse Event System Organ Class>>				
<Programming note: sort by number of subjects so that the AE System Organ Classes and Preferred Terms with the highest frequencies appear first>	XXX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
<<Adverse Event Preferred Term>>	XXX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
<<Adverse Event Preferred Term>>	XXX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)

Note: Table entries are number (%) of subjects.

Treatment-emergent AE is defined as any AE with an onset date on or after the first study product administration date. Counts reflect numbers of subjects reporting one or more adverse events that map to the MedDRA (version 22.0) system organ class or preferred term. A subject may be counted once only in each row at the most severe rating.

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Listing 16.1.7: Subject Randomization
All Randomized Subjects

Subject Number	Informed Consent Date	Randomization Date	Randomization Number	Randomization [1]	
				Site 1	Site 2
XX	XXXX-XX-XX	XXXX-XX-XX	XX	A	B
XX	XXXX-XX-XX	XXXX-XX-XX	XX	B	A
XX	XXXX-XX-XX	XXXX-XX-XX	XX	B	A
XX	XXXX-XX-XX	XXXX-XX-XX	XX	B	A
XX	XXXX-XX-XX	XXXX-XX-XX	XX	B	A

[1] A = MC2-01 Cream; B = MC2-01 Vehicle

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Listing 16.2.1: Subject Disposition and Population Inclusion
All Randomized Subjects

	Date (Day [1]) of				Analysis Population	
Subject Number	**Screening**	**Day 1**	**Last Visit or Contact**	**End of Study Status**	**Completed Study (Phototoxicity Analysis)**	**Safety**
XX	XXXX-XX-XX	XXXX-XX-XX	XXXX-XX-XX (X)	COMPLETED	Y	Y
XX	XXXX-XX-XX	XXXX-XX-XX	XXXX-XX-XX (X)	COMPLETED	Y	Y
XX	XXXX-XX-XX	XXXX-XX-XX	XXXX-XX-XX (X)	SUBJECT IS LOST TO FOLLOW-UP	N	Y
XX	XXXX-XX-XX	XXXX-XX-XX	XXXX-XX-XX (X)	COMPLETED	Y	Y
XX	XXXX-XX-XX	XXXX-XX-XX	XXXX-XX-XX (X)	INVESTIGATOR'S JUDGEMENT	Y	Y

[1] Study day is relative to Day 1.

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Listing 16.2.2: Protocol Deviations
All Randomized Subjects

Subject Number	Protocol Deviation Description	Type
xx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	xxxxxxxxxx
xx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	xxxxxxxxxx
xx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	xxxxxxxxxx

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Listing 16.2.4.1: Demographics and Baseline Characteristics
All Randomized Subjects

Subject Number	Date of Birth	Age (Years) [1]	Gender	Race	Ethnicity	Fitzpatrick Skin Type [2]
xx	xxxx-xx-xx	xx	xxxxxx	xxxxxxxxxxxx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxx	I
xx	xxxx-xx-xx	xx	xxxxxx	xxxxxx	xxxxxxxxxxxxxxxxxxxxxx	III
xx	xxxx-xx-xx	xx	xxxxxx	Other: xxxxxxxxxxxxx	xxxxxxxxxxxxxxxxxxxxx	II
xx	xxxx-xx-xx	xx	xxxxxx	xxxxxx	xxxxxxxxxxxxxxxxxxxxxxx	I

[1] Age is relative to Day 1.
[2] I = Always burns easily, never tans; II = Always burns easily, tans minimally; III = Burns moderately, tans gradually

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Listing 16.2.4.2: Medical History
All Randomized Subjects

Subject Number	Diagnosis and/or Procedure	Onset Date	Resolution Date
xx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	XXXX	XXXX-XX-XX
	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	XXXX-XX-XX	Ongoing
xx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	XXXX-XX-XX	XXXX-XX-XX
xx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	XXXX-XX	Ongoing

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Listing 16.2.4.3: Prior and Concomitant Medications
All Randomized Subjects

Subject Number	WHO Preferred Term (Verbatim Term) / ATC Classification	Indication / Dose / Unit / Route / Frequency	Start Date (Day) – Stop Date (Day)
XX	XXXXXXXX (XXXXXX) / XXXXXXXXXXXXXXXXXXXXXXXXXXXXX	XXXXXXXXXXXXXXX / XXXXX / XX / XXXX/ XXXX	XXXX-XX-XX (XX) – XXXX-XX-XX (XX)
	XXXXXXXX (XXXXXX) / XXXXXXXXXXXXXXXXXXXXXXXXXXXXX	XXXXXXXXXXXXXXX / XXXXX / XX / XXXX/ XXXX	XXXX – Ongoing
XX	XXXXXXXX (XXXXXX) / XXXXXXXXXXXXXXXXXXXXXXXXXXXXX	XXXXXXXXXXXXXXX / XXXXX / XX / XXXX/ XXXX	XXXX – XXXX-XX-XX (XX)

Note: Study day is calculated relative to Baseline (Day 1).

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Listing 16.2.5: MED Determination
All Randomized Subjects

Subject Number	Date-Time of Irradiation	Time Point Post-Irradiation	Date-Time of Reading		Subsite 1	2	3	4	5	6	MED
xx	xxxx-xx-xxTxx:xx			UVB/UVA Intensity ($\mu W/cm^2$)	xx	xx	xx	xx	xx	xx	
				Exposure (seconds)	xx	xx	xx	xx	xx	xx	
		Immediate	xxxx-xx-xxTxx:xx	Reading	xx	xx	xx	xx	xx	xx	
		16 – 24 Hours	xxxx-xx-xxTxx:xx	Reading	xx	xx	xx	xx	xx	xx	x.xx
xx	xxxx-xx-xxTxx:xx			UVB/UVA Intensity ($\mu W/cm^2$)	xx	xx	xx	xx	xx	xx	
				Exposure (seconds)	xx	xx	xx	xx	xx	xx	
		Immediate	xxxx-xx-xxTxx:xx	Reading	xx	xx	xx	xx	xx	xx	
		16 – 24 Hours	xxxx-xx-xxTxx:xx	Reading	xx	xx	xx	xx	xx	xx	x.xx

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Listing 16.2.6: Assessment of Dermal Responses
All Randomized Subjects

								MC2-01 Cream		MC2-01 Vehicle		Untreated	Re-test Needed
								Erythema/Edema Notation		Erythema/Edema Notation		Erythema/ Edema Notation	
Subject Number	**Date-Time of Application**	**½ MED UVB/UVA (sec.)**	**16 J/cm² UVA (sec.)**	**UVB/ UVA (µW/cm²)**	**UVA (mW / cm²)**	**Time Point Post-Irradiation**	**Date-Time of Reading/ Assessment**	**Irr**	**Non-Irr**	**Irr**	**Non-Irr**	**Irr**	**Y/N**
xx	xxxx-xx-xx Txx:xx	xx.xx	xx.xx	xx.xx	xx.xx	0 hrs (Day 2)	xxxx-xx-xx Txx:xx	xx/xx	xx/xx	xx/xx	xx/xx	xx/xx	
						24 hrs (Day 3)	xxxx-xx-xx Txx:xx	xx/xx	xx/xx	xx/xx	xx/xx	xx/xx	
						48 hrs (Day 4)	xxxx-xx-xx Txx:xx	xx/xx Hr	xx/xx	xx/xx Hr	xx/xx	xx/xx	Y
						Photo-Toxicity Reaction Assessment	xxxx-xx-xx	Xxx		Xxx			

Scores:
Erythema: 0 = No reaction; 1 = Mild, but definite erythema; 2 = Moderate erythema; 3 = Marked/severe erythema;
Edema: 0 = No reaction; 1 = Mild, but definite edema; 2 = Definite edema with erosion/vesiculation

Notations:
Hr = hyperpigmentation; Ho = hypopigmentation; V = vesiculation; p= Papular response; pv= Papulovesicular response; D= Damage to epidermis; oozing, crusting, and/or superficial erosions; I=Itching; S= Spreading of reaction beyond patch study site (i.e., reaction where material did not contact skin); f= Follicular irritation with or without pustule formation (folliculitis).; X=Subject absent; PD=Patch dislodged; NP = Not Patched ; 0=No Reaction
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[A similar listing will be produced for Re-Test Skin Assessments as needed],

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Listing 16.2.7.1: Adverse Events
All Randomized Subjects

Subject Number	MedDRA Term (Verbatim Term) / MedDRA SOC Term	Treatment-emergent? / Date (Day) of Onset – Date of Resolution (Day)	Intensity / Relationship / Outcome	Action Taken with Study Drug / Action Taken to Treat the Event? / Serious Adverse Event (SAE)?
xx	XXXXXXXX (XXXXXX) / XXXXXXXXXX	Yes / xxxx-xx-xx (xx) – xxxx-xx-xx (xx)	Severe / Possible / Recovered	Dose reduced / Yes / Yes
	XXXXXXXX (XXXXXX) / XXXXXXXXXX	No / xxxx-xx-xx (xx) – Ongoing	Mild / Not related / Unknown	Dose not changed / No / No
xx	XXXXXXXX (XXXXXX) / XXXXXXXXXX	Yes / xxxx-xx-xx (xx) – xxxx-xx-xx (xx)	Moderate / Not related/ Recovered	Dose not changed / No / No

Note: A treatment-emergent AE is an AE with an onset date on or after the first study product administration date. Study day is relative to Day 1.
<Programming Note: Insert a comment column if comments related to this listing were recorded in the data.>
Generated on XX/XX/XX:XXXX by XXXXXXX / Uses: XXXX, XXXX

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Listing 16.2.7.2: Serious Adverse Events and Deaths
All Randomized Subjects

Subject Number	MedDRA Term (Verbatim Term) / MedDRA SOC Term	Treatment-emergent? / Date (Day) of Onset – Date of Resolution (Day)	Intensity / Relationship / Outcome	Action Taken with Study Drug / Action Taken to Treat the Event? / Which Criteria Met?
xx	xxxxxxxxx	Yes / xxxx-xx-xx (xx) – xxxx-xx-xx (xx)	Severe / Possibly Related / Recovering	Dose reduced / Yes / Hospitalization
	xxxxxxxxx	No / xxxx-xx-xx (xx) – Ongoing	Mild / Not related / Unknown	Dose not changed / No / Other Medically Serious Event
xx	xxxxxxxxx	Yes / xxxx-xx-xx (xx) – xxxx-xx-xx (xx)	Moderate / Probably related / Recovered	Drug withdrawn / No / Other Medically Serious Event

Note: A treatment-emergent AE is an AE with an onset date on or after the first study product administration date. Study day is relative to Day 1.
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Listing 16.2.8: Urine Pregnancy Test Results
All Randomized Female Subjects

Subject Number	Childbearing Potential	Urine Pregnancy Test			
		Day 1		End of Study	
		Date	Result	Date	Result
xx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	xxxx-xx-xx	Negative	xxxx-xx-xx	Negative
xx	Postmenopausal	--	N/A	--	N/A

Generated on XX/XX/XX:XXXX by XXXXXXX / Uses: XXXX, XXXX

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Listing 16.2.9: Comments
All Randomized Subjects

Subject Number	Reference	Comment
xx	GENERAL COMMENTS	XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX
	END OF STUDY	XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX
xx	GENERAL COMMENTS	XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX

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