ORIGINAL

TSCA NON-CONFIDENTIAL BUSINESS INFORMATION

DOCUMENT DESCRIPTION	DOCUMENT CONTROL NUMBER	DATE RECEIVED
FYI-13-01704	84130000007	2/12/13

COMMENTS:

DOES NOT CONTAIN CBI

351958

Shin-Etsu

Shin-Etsu MicroSi, Inc.

February 6, 2013

2013 FEB 12 AM 6:02

RECEIVED
OPPT CBIC

TSCA Confidential Business Information Center (7407M)
EPA East - Room 6428 Attn: FYI
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, DC 20460-0001

FYI-13-01704

RE: TSCA FYI submission of an Acute dermal toxicity study of HMDS in NZW rabbits.

To Whom It May Concern,

Shin-Etsu MicroSi is providing the attached Acute Dermal toxicity study of HMDS in NZW rabbits as an "FYI" submittal to the EPA.

Study Objective: To determine the Acute Dermal Rabbit LD50 of HMDS. The LD50 is used to determine whether this chemical meets the Toxic criteria in the Department of Transportation (DOT) shipping regulations.

Chemical identity:

Chemical name: Hexamethyldisilazane

Shin-Etsu MicroSi alias name: HMDS

CAS RN: 999-97-3

Please contact me at 480-893-8898 or jedmonds@microsi.com for questions regarding this submittal.

Thank you,

84130000007

Jim Edmonds, President

February 6, 2013
Date

CONTAINS NO CBI

www.MICROSI.COM
480.893.8898 | FAX 480.893.8637
10028 S. 51ST STREET | PHOENIX, AZ 85044

D2D DRIVEN TO DELIVER

Final Report

TBH-1166 (KG-2012-384)

HMDS

Acute dermal toxicity study of HMDS in NZW rabbits

KOREA TESTING & RESEARCH INSTITUTE

Ki Sung Cho

GLP Statement

Study title : Acute dermal toxicity study of HMDS in NZW rabbits

Study number : TBH-1166 (KG-2012-384)

Sponor

Name : Shin-Etus MicroSi
Address : #10028 S, 51st Street, Phoenix, Arizona, USA.
Representative : Greg Fisher
Contact Number : Tel. +602-770-6961

Test facility

Name : Health Care Research Laboratory, Korea Testing & Research Institute (KTR)
Address : 7-6, Gomak-ri, Wolgot-myeon, Gimpo-si, Gyunggi-do, 415-871, Korea

Management : Kim Ki-sung
Contact Number : Tel. +82-31-999-3214 Fax. +82-31-999-3003

This study was conducted under the supervision of the study director and is in compliance with the principles of Good Laboratory Practice.

1. Good Laboratory Practice

1.1. OECD Principle of Good Laboratory Practice, ENV/MC/CHEM (98)17 (as revised in 1997)

2. Test regulation

2.1. OECD Guideline for testing of chemicals, TG 402 (Adopted; 24 Feb 1987) "Acute Dermal Toxicity"

This study was conducted in compliance with the study plan, and this report provides a true and accurate record of the results obtained.

Shin Sung-sup 2012-10-31

Shin Sung-sup B.S. Date
Study director
Health Care Research Laboratory, KTR

Quality Assurance Statement

Study title : Acute dermal toxicity study of HMDS in NZW rabbits

Study title : TBH-1166 (KG-2012-384)

Study Phases	Date of QA inspections	Date of reports to the SD	Date of reports to the management
Draft study plan audit	2012-08-22	2012-08-22	2012-08-22
Study plan audit	2012-08-23	2012-08-23	2012-08-23
Animal receipt audit	2012-09-13	2012-09-14	2012-09-14
Group allocation audit	2012-09-19	2012-09-19	2012-09-19
Body weight audit	2012-09-20	2012-09-20	2012-09-20
Preparation/storage of test substance and vehicle audit	2012-09-20	2012-09-20	2012-09-20
Administration of test substance audit	2012-09-20	2012-09-20	2012-09-20
Necropsy findings audit(2)	2012-10-04	2012-10-04	2012-10-04
Raw data audit	2012-10-17	2012-10-17	2012-10-17
Draft report audit	2012-10-17	2012-10-17	2012-10-17
Final report audit	2012-10-31	2012-10-31	2012-10-31

Inspection of the routine and repetitive procedures that constitute the study was carried out as a continuous process designed to encompass the major phases at or about the time this study was in progress.

This report has been audited by KTR Quality Assurance Unit, and is considered to be an accurate account of the raw data generated and of the procedures followed.

Inspections were accomplished as noted, and reported to the study director and management immediately following their completion. Based on these inspections and the review of the report, this study was conducted and reported in conformance with the Good Laboratory Practice regulations.

Park Jong Il

Park Jong-il, Ph.D. Candidate
Quality Assurance Manager
Health Care Research Laboratory, KTR

2012-10-31

Date

Study Staffs

Following staffs conducted in compliance with the KTR SOPs and the study plan of this study

Study personnel	: Kim Jun-ho/B.S. Lee Teak-jin/B.S.
Test substance preparation	: Yang Ji-a/B.S Jung Jung-wook/B.S Kim Min-seok/B.S
Animal care manager	: Park Hak-su/D.V.M., Ph.D. Candidate
Quarantine manager	: Shin Sung-sup/B.S.
Statistics of data	: Shin Sung-sup/B.S.
Drawing of report	: Shin Sung-sup/B.S.

Contents

Report cover
GLP Statement I
Quality Assurance Statement II
Study Staffs III
Contents IV
1. Summary 1
2. Introduction 2
2.1. Study schedule 2
3. Materials & methods 3
3.1. Test substance and vehicle 3
3.2. Preparation of test substance 3
3.3. Analysis of test substance 3
3.4. Test system 3
3.5. Animal husbandry 5
3.6. Allocation 5
3.7. Administration of test substances 6
3.8. Observations 6
3.9. Statistical analysis 6
4. Archives 7
5. Amendments and deviations from the study plan 7
6. Results 8
6.1. Mortality and clinical signs 8
6.2. Body weight changes 8
6.3. Necropsy findings 8
7. Discussion & conclusion 9
8. References 10
9. Tables (Group summary) 11
Table 1. Mortality 11
Table 2. Clinical signs 11
Table 3. Body weight 12
Table 4. Necropsy findings 12
10. Appendices (Individual data) 13
Appendix 1. Clinical signs of male rabbits 13
Appendix 2. Clinical signs of female rabbits 15
Appendix 3. Body weight of male rabbits 17

Appendix 4. Body weight of female rabbits 18
Appendix 5. Necropsy findings of male rabbits 19
Appendix 6. Necropsy findings of female rabbits 21
11. Annexes 22
Annex 1. Information of test substance (Submitted by sponsor) 22
Annex 2. Certificate of analysis (Submitted by sponsor) 24
Annex 3. Amendment document of study plan 25

1. Summary

The present study, to investigate acute dermal toxicity study of HMDS was conducted to the NZW rabbits. The high dose of test substance, 1000 mg/kg body weight was established according to sponsor request. Middle and low dose was designed 500 and 250 mg/kg body weight, respectively. The control group was administered to conditioned media not containing extract. After single dose administration of acute dermal Mortality, clinical signs, body weight and necropsy findings were observed for 14 days.

- No mortality was observed in the present study.
- Erythema was observed 1 (1/5) case in male 250 mg/kg B.W. group and 4 (4/5)case in female 250 mg/kg B.W. group and all case in 500 (5/5), 1000 (5/5) mg/kg B.W. group from 1 days to 3 days after administration in both sexes, and crust formation was observed from 4 days to 14 days after administration.
- No statistically significant change in body weight was observed between the treatment and vehicle control groups.
- In necropsy findings, crust formation at administration site was observed all case in 500, 1000 mg/kg B.W. group in both sexes, and otherwise no toxicological changes related to administration of test substance.

Based on these results, the LD_{50} value of the HMDS was considered to be higher than 1000 mg/kg body weight in NZW rabbit.

2. Introduction

This study was executed to evaluate acute dermal toxicity of the HMDS in NZW rabbit. Dermal route was for treatment route because major exposure route of HMDS was dermal.

This study was conducted in accordance with the regulation for the care and use of laboratory animals of Korea Testing & Research Institute (revised adopted December 10, 2010 by institutional animal care and use committee).

2.1 Study schedule

Study Initiation	:	2012-09-12
Animal receipt	:	2012-09-13
Quarantine and acclimatization periods	:	2102-09-13 ~ 2012-09-19
Administration	:	2012-09-20
Observation periods	:	2012-09-20 ~ 2012-10-04
Necropsy	:	2012-10-04
Draft final report	:	2102-10-17
Study completion	:	2012-10-31

3. Materials & Methods

3.1 Test substance and vehicle

3.1.1 Test substance (Annex 1.)

Name	:	HMDS
Supplier	:	Shin-Etus MicroSi
Manufacturing date	:	2012-06-28
Delivery amount	:	677.570 g (Gross)
Cas No.	:	999-97-3
Physical description	:	Liquid solvent
Purity	:	〉 99 %

3.1.2 Vehicle

Name	:	Corn oil
Manufactured by	:	Sigma-Aldrich Corporation
Lot No.	:	MKBF6012V

3.2 Preparation of test substance

Test substance was suspended at final concentration of 125, 250 and 500 mg/mL in corn oil solution using the weighing factor given above. The mixture of the test substance was homogenized by shaking.

3.3 Analysis of test substance

Based on certificate of analysis about the individual dose furnished by sponsor, the test for stability, homogenization and content of manufactured test substance was not carried out separately.

3.4 Test system

Animal strain and species : Yac:NZW(KBL), Rabbit
Supplier : Cheonan Yonam college
(Suhyang-ri, Seonghwan-eup, Seobuk-gu, Cheonan-si, Chungcheongnam-do, Korea)
No. of animal and sex distinction at the time of receipt : 22 males / 22 females
A range of age and body weight at the time of receipt :
About 3 month old, male 1721.2 g ~ 2019.0 g / female 1768.6 g ~ 2099.5 g
No. of animal and sex distinction at the time of administration : 20 males / 20 females
A range of age and body weight at the time of administration :
about 3 month old, males 2000.7 g ~ 2196.9 g / females 2036.1 g ~ 2296.2 g

3.4.1 Reason for selection of the animal

The NZW rabbit is commonly used for various field of toxicology study, and the interpretation and assessment of the results is easy because there is a plenty of reference data.

3.4.2 Quarantine and acclimation

On receipt the animals were examined for any signs of healthy or injury. The animals were acclimated for 7 days when their health status was assessed. A total of 44 animals were accepted into the study.

3.4.3 Identification of animals

Identification cards including information such as study number, test substance name, test title, receipt date, quarantine period, allocation date, experimental period, sex, group number and study director's name.

3.4.4 Group allocation

The healthy animals without abnormal sign and with normal body weight gain during the quarantine and acclimation period that were selected.

3.4.5 Remnant animal

Remnant animals were test terminated

3.5 Animal husbandry

3.5.1 Environmental conditions [Rabbit room No. 2]

The room environmental was controlled [(target conditions : temperature (20 ± 3) ℃, relative humidity (50 ± 20) %. The rate of air exchange was at least (10 ~ 15) times air changes per hour and lighting was automatically controlled to provide 12 hours of artificial light (08:00 ~ 20:00 hours, 150 ~ 300Lux)] in the animal room. The feed and water were supplied for acclimation and test period.

3.5.2 Environmental monitoring

The temperatures and relative humidities was continuously monitored per 30 minute by a computerized system. The luminous intensity measured according to KTR SOP periodically. The environmental conditions were not thought to have affected the purpose or integrity of the study.

3.5.3 Housing

The animals were housed in stainless steel cages [380(W)×480(D)×300(H)㎜, Jeongdo Ltd., Korea].

3.5.4 Food and water

The animals were fed pallet diet for rabbit (Cargill agri purina, Inc., 56-4, Soryong-dong, Gunsan-si, Jeonbuk, Korea) and given the filtered and UV irradiated water *ad libitum*.

3.5.5 Confirmation of the absence of contamination for food and water

The contaminant of feed was confirmed from feed supplier receives by feed certificate of analysis (COA) which follows in periodical of feed manufacturing industry. The water was considered not to contain any contaminant at a level that has affected the purpose of integrity of the study by the periodical inspection which in the corresponding SOPs of KTR Health Care Research Laboratory.

3.6 Allocation

3.6.1 Full study

The high dose, 1000 mg/kg B.W. was established according to the results of preliminary test study data(Study No. TBH-1310_Non GLP). Middle and low dose was designed 500 and 250 mg/kg, respectively. The control group was administered to vehicle control, corn oil solution.

Group	Test substance	Sex	Number of animal	Animal number	Dose levels (mg/kg B.W.)	Dosing volume (mL/kg B.W.)
G 1	Corn oil (Vehicle)	Male	5	1101 ~ 1105	0	2
		Female	5	2101 ~ 2105		
G 2	HMDS (Low Dose)	Male	5	1201 ~ 1205	250	2
		Female	5	2201 ~ 2205		
G 3	HMDS (Middle Dose)	Male	5	1301 ~ 1305	500	2
		Female	5	2301 ~ 2305		
G 4	HMDS (High Dose)	Male	5	1401 ~ 1405	1000	2
		Female	5	2401 ~ 2405		

3.7 Administration of test substance

3.7.1 Administration route

The test substance, HMDS was administrated dermally as the clinical route is dermal.

3.7.2 Administration method

The hair of back region of animals was removed (about 10%) harmlessly to treat the test substance before administration day. The area of administration was about 10 % (rabbit : 15cm × 15cm) of body surface area. Test substance should be held in contact with the skin with a porous gauze dressing and non-irritating tape(Tegarderm, 3M) throughout a 24-hour exposure period. The test site should be further covered in a suitable manner to retain the gauze dressing and test substance and ensure that the animals cannot ingest the test substance. At the end of the exposure period, residual test substance should be removed, where practicable using water.

3.8 Administration volume

The administration volume was calculated to 2.0 mL/kg body weight

3.9 Observations

3.9.1 Clinical signs

Clinical signs were carefully observed for 4 hours after treatment and then an once everyday for 14 days.

3.9.2 Changes of body weight

Body weight was measured animal receipt day, animal allocation day, just before treatment and on day 7 and 14 after the administration.

3.9.3 Necropsy findings

On the end of study period, all animals were sacrificed by bloodletting ether anesthesia. Autopsy was conducted on all animals and the organs were examine for gross lesions.

3.10 Statistical analysis

The body weights was analyzed for homogeneity of variances using Levene's test. One way ANOVA analysis was performed to evaluate the significance of differences. All statistical analysis will be performed using SPSS program.

4. Archives

All records created during this study period was archived in the storage facility (I) of KTR Health Care Research Laboratory. Test substance was archived in the storage facility (II) for 5 years after in issuance of final report. After storage period, additional period for records and test substance will be determined by consultation with sponsors.

5. Amendments and deviations from the study plan

5.1 Information for Management

Management change depending on the "Change in personnel (Personnel order No. 47, 2012-09-11)" Before : Park Gil-jong / After : Kim Ki-sung

5.2 Other

In addition to information for management, There were not additional amendments or deviations from the protocol of this study.

6. Results

6.1 Mortality and Clinical signs (Table 1, 2 and Appendix 1)

No death occurred in the all animals during the experimental period. The clinical signs related with the Erythema was observed 1 (1/5) case in male 250 mg/kg B.W. group and 4 (4/5)case in female 250 mg/kg B.W. group and all case in 500 (5/5), 1000 (5/5) mg/kg B.W. group from 1 days to 3 days after administration in both sexes, and crust formation was observed from 4 days to 14 days after administration.

6.2 Body weight changes (Table 3, Appendix 2)

No statistically significant change in body weight was observed between the treatment and vehicle control groups.

6.3 Necropsy findings (Table 4, Appendix 3)

In necropsy findings, crust formation at administration site was observed all case in 500, 1000 mg/kg B.W. group in both sexes, and otherwise no toxicological changes related to administration of test substance.

7. Discussion & Conclusion

The present study, to investigate acute dermal toxicity study of HMDS was conducted to the NZW rabbits. The high dose of test substance, 1000 mg/kg body weight was established according to sponsor request. Middle and low dose was designed 500 and 250 mg/kg body weight, respectively. The control group was administered to conditioned media not containing extract. After single dose administration of acute dermal Mortality, clinical signs, body weights and necropsy findings were observed for 14 days.

No mortality was observed in the present study. Erythema was observed 1 (1/5) case in male 250 mg/kg B.W. group and 4 (4/5)case in female 250 mg/kg B.W. group and all case in 500 (5/5), 1000 (5/5) mg/kg B.W. group from 1 days to 3 days after administration in both sexes, and crust formation was observed from 4 days to 14 days after administration. No statistically significant change in body weights was observed between the treatment and vehicle control groups. In necropsy findings, crust formation at administration site was observed all case in 500, 1000 mg/kg B.W. group in both sexes, and otherwise no toxicological changes related to administration of test substance.

Based on these results, the LD_{50} value of the HMDS was considered to be higher than 1000 mg/kg body weight in NZW rabbit.

8. References

- OECD Guideline for testing of chemicals, TG 402 (Adopted; 24 Feb 1987) "Acute Dermal Toxicity"

- OECD Principle of Good Laboratory Practice, ENV/MC/CHEM (98)17 (as revised in 1997)

9. Tables (Group summary)

Table 1 . Mortality

Group	Dose (mg/kg)	Mortality (dead / total)	
		Male	Female
G1	0	0% (0 / 5)[a]	0% (0 / 5)
G2	250	0% (0 / 5)	0% (0 / 5)
G3	500	0% (0 / 5)	0% (0 / 5)
G4	1000	0% (0 / 5)	0% (0 / 5)

[a] : No. of dead animals / No. of tested animals

Table 2 . Clinical signs

Group	Dose (mg/kg)	Sex	Number of animals	Clinical signs
G1	0	Male	5	NAD
		Female	5	NAD
G2	250	Male	4	NAD
			1	Erythema
		Female	1	NAD
			4	Erythema
G3	500	Male	5	Erythema, Crust formation
		Female	5	Erythema, Crust formation
G4	1000	Male	5	Erythema, Crust formation
		Female	5	Erythema, Crust formation

NAD: No abnormalities detected

Table 3. Body weights

Unit : g

Group	Dose (mg/kg)	Sex		Days after administration		
				0	7	14
G1	0	Male	Mean	2091.2	2351.6	2482.7
			S.D.	64.2	121.8	156.0
			N	5	5	5
		Female	Mean	2154.5	2423.0	2588.7
			S.D.	101.2	117.5	92.3
			N	5	5	5
G2	250	Male	Mean	2104.4	2355.1	2520.4
			S.D.	65.5	102.2	110.8
			N	5	5	5
		Female	Mean	2106.2	2389.3	2568.1
			S.D.	17.7	26.4	104.3
			N	5	5	5
G3	500	Male	Mean	2071.4	2359.3	2509.2
			S.D.	58.8	57.7	84.5
			N	5	5	5
		Female	Mean	2097.4	2333.8	2547.4
			S.D.	46.8	62.1	126.0
			N	5	5	5
G4	1000	Male	Mean	2085.6	2294.4	2417.3
			S.D.	23.4	98.7	116.6
			N	5	5	5
		Female	Mean	2129.2	2348.7	2513.3
			S.D.	91.3	162.4	189.6
			N	5	5	5

N : No. of animals, S.D. : Standard deviation

Table 4. Necropsy findings

Findings	Group (mg/kg)							
	G1 (0)		G2 (250)		G3 (500)		G4 (1000)	
	Male	Female	Male	Female	Male	Female	Male	Female
Number of examined	5	5	5	5	5	5	5	5
NAD	5	5	5	5	0	0	0	0
Crust formation	0	0	0	0	5	5	5	5

NAD: No abnormalities detected,

10. Appendices (Individual data)

Appendix 1. Clinical signs of male rabbits

Group	Dose (mg/kg)	Animal number	Hours after administration				Days after administration			
			1 h	2 h	3 h	4 h	1	2	3	4
G1	0	1101	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD
		1102	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD
		1103	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD
		1104	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD
		1105	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD
G2	250	1201	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD
		1202	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD
		1203	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD
		1204	NAD	NAD	NAD	NAD	K11(09, 01)	K11(09, 01)	K11(09, 01)	NAD
		1205	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD
G3	500	1301	NAD	NAD	NAD	NAD	K11(09, 01)	K11(09, 01)	K11(09, 01)	K34(09, 01)
		1302	NAD	NAD	NAD	NAD	K11(09, 01)	K11(09, 01)	K11(09, 01)	K34(09, 01)
		1303	NAD	NAD	NAD	NAD	K11(09, 01)	K11(09, 01)	K11(09, 01)	K34(09, 01)
		1304	NAD	NAD	NAD	NAD	K11(09, 01)	K11(09, 01)	K11(09, 01)	K34(09, 01)
		1305	NAD	NAD	NAD	NAD	K11(09, 01)	K11(09, 01)	K11(09, 01)	K34(09, 01)
G4	1000	1401	NAD	NAD	NAD	NAD	K11(09, 01)	K11(09, 01)	K11(09, 01)	K11(09, 01)
		1402	NAD	NAD	NAD	NAD	K11(09, 01)	K11(09, 01)	K11(09, 01)	K11(09, 01), K34(09, 01)
		1403	NAD	NAD	NAD	NAD	K11(09, 01), K34(09, 01)	K11(09, 01), K34(09, 01)	K11(09, 01), K34(09, 01)	K34(09, 01)
		1404	NAD	NAD	NAD	NAD	K11(09, 02), K34(09, 02)	K11(09, 02), K34(09, 02)	K11(09, 02), K34(09, 02)	K34(09, 02)
		1405	NAD	NAD	NAD	NAD	K11(09, 01), K34(09, 01)	K11(09, 01), K34(09, 01)	K11(09, 01), K34(09, 01)	K34(09, 02)

NAD: No abnormalities detected, K11(09, 01, 02) : Erythema(09-Administration site, 01-Slight, 02-Moderate), K34(09, 01, 02) : Crust formation(09-Administration site, 01-Slight, 02-Moderate)

Appendix 1. (Continued) Clinical signs of male rabbits

Group	Dose (mg/kg)	Animal number	Days after administration									
			5	6	7	8	9	10	11	12	13	14
G1	0	1101	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD
		1102	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD
		1103	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD
		1104	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD
		1105	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD
G2	250	1201	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD
		1202	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD
		1203	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD
		1204	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD
		1205	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD
G3	500	1301	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)
		1302	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)
		1303	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)
		1304	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)
		1305	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)
G4	1000	1401	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)
		1402	K11(09, 01), K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)
		1403	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)
		1404	K34(09, 02)	K34(09, 02)	K34(09, 02)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)
		1405	K34(09, 02)	K34(09, 02)	K34(09, 02)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)

NAD: No abnormalities detected, K11(09, 01) : Erythema(09-Administration site, 01-Slight),
K34(09, 01, 02) : Crust formation(09-Administration site, 01-Slight, 02-Moderate)

(End)

Appendix 2. Clinical signs of female rabbits

Group	Dose (mg/kg)	Animal number	Hours after administration				Days after administration			
			1 h	2 h	3 h	4 h	1	2	3	4
G1	0	2101	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD
		2102	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD
		2103	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD
		2104	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD
		2105	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD
G2	250	2201	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD
		2202	NAD	NAD	NAD	NAD	K11(09, 01)	K11(09, 01)	K11(09, 01)	NAD
		2203	NAD	NAD	NAD	NAD	K11(09, 01)	K11(09, 01)	K11(09, 01)	NAD
		2204	NAD	NAD	NAD	NAD	K11(09, 01)	K11(09, 01)	K11(09, 01)	NAD
		2205	NAD	NAD	NAD	NAD	K11(09, 01)	K11(09, 01)	K11(09, 01)	NAD
G3	500	2301	NAD	NAD	NAD	NAD	K11(09, 02)	K11(09, 02)	K11(09, 02)	K34(09, 01)
		2302	NAD	NAD	NAD	NAD	K11(09, 02)	K11(09, 02)	K11(09, 02)	K34(09, 01)
		2303	NAD	NAD	NAD	NAD	K11(09, 02), K34(09, 01)	K11(09, 02), K34(09, 01)	K11(09, 02), K34(09, 01)	K34(09, 01)
		2304	NAD	NAD	NAD	NAD	K11(09, 02), K34(09, 01)	K11(09, 02), K34(09, 01)	K11(09, 02), K34(09, 01)	K34(09, 01)
		2305	NAD	NAD	NAD	NAD	K11(09, 02), K34(09, 01)	K11(09, 02), K34(09, 01)	K11(09, 02), K34(09, 01)	K34(09, 02)
G4	1000	2401	NAD	NAD	NAD	NAD	K11(09, 03), K34(09, 03)	K11(09, 03), K34(09, 03)	K11(09, 03), K34(09, 03)	K34(09, 02)
		2402	NAD	NAD	NAD	NAD	K11(09, 03), K34(09, 03)	K11(09, 03), K34(09, 03)	K11(09, 03), K34(09, 03)	K34(09, 03)
		2403	NAD	NAD	NAD	NAD	K11(09, 03), K34(09, 03)	K11(09, 03), K34(09, 03)	K11(09, 03), K34(09, 03)	K34(09, 03)
		2404	NAD	NAD	NAD	NAD	K11(09, 03), K34(09, 03)	K11(09, 03), K34(09, 03)	K11(09, 03), K34(09, 03)	K34(09, 03)
		2405	NAD	NAD	NAD	NAD	K11(09, 03), K34(09, 03)	K11(09, 03), K34(09, 03)	K11(09, 03), K34(09, 03)	K34(09, 03)

NAD: No abnormalities detected, K11(09, 01, 02, 03): Erythema(09-Administration site, 01-Slight, 02-Moderate, 03 -Severe), K34(09, 01, 02, 03):Crust formation(09-Administration site, 01-Slight, 02-Moderate, 03-Severe)

Appendix 2. (Continued) Clinical signs of female rabbits

Group	Dose (mg/kg)	Animal number	Days after administration									
			5	6	7	8	9	10	11	12	13	14
G1	0	2101	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD
		2102	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD
		2103	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD
		2104	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD
		2105	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD
G2	250	2201	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD
		2202	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD
		2203	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD
		2204	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD
		2205	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD	NAD
G3	500	2301	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)
		2302	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)
		2303	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)
		2304	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)
		2305	K34(09, 02)	K34(09, 02)	K34(09, 02)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)	K34(09, 01)
G4	1000	2401	K34(09, 02)	K34(09, 02)	K34(09, 02)	K34(09, 02)	K34(09, 02)	K34(09, 02)	K34(09, 02)	K34(09, 02)	K34(09, 02)	K34(09, 02)
		2402	K34(09, 03)	K34(09, 03)	K34(09, 02)	K34(09, 02)	K34(09, 02)	K34(09, 02)	K34(09, 02)	K34(09, 02)	K34(09, 02)	K34(09, 02)
		2403	K34(09, 03)	K34(09, 03)	K34(09, 02)	K34(09, 02)	K34(09, 02)	K34(09, 02)	K34(09, 02)	K34(09, 02)	K34(09, 02)	K34(09, 02)
		2404	K34(09, 03)	K34(09, 03)	K34(09, 03)	K34(09, 03)	K34(09, 03)	K34(09, 02)	K34(09, 02)	K34(09, 02)	K34(09, 02)	K34(09, 02)
		2405	K34(09, 03)	K34(09, 03)	K34(09, 03)	K34(09, 03)	K34(09, 03)	K34(09, 02)	K34(09, 02)	K34(09, 02)	K34(09, 02)	K34(09, 02)

NAD: No abnormalities detected, K34(09, 01, 02) : Crust formation(09-Administration site, 01-Slight, 02-Moderate, 03-Severe)

(End)

Appendix 3. Body weight of male rabbits

unit : g

Group	Dose (mg/kg)	No.	Days after administration		
			0	7	14
G1	0	1101	2162.7	2416.0	2529.3
		1102	2093.7	2306.7	2465.8
		1103	2006.7	2186.1	2236.0
		1104	2142.2	2511.6	2663.5
		1105	2050.7	2337.4	2519.0
		Mean	2091.2	2351.6	2482.7
		S.D.	64.2	121.8	156.0
G2	250	1201	2107.7	2453.3	2601.2
		1202	2011.8	2194.9	2341.5
		1203	2103.5	2401.4	2537.1
		1204	2101.9	2317.0	2502.2
		1205	2196.9	2408.8	2620.1
		Mean	2104.4	2355.1	2520.4
		S.D.	65.5	102.2	110.8
G3	500	1301	2053.4	2362.4	2504.6
		1302	2163.7	2435.1	2596.2
		1303	2068.2	2351.5	2498.5
		1304	2000.7	2274.0	2377.8
		1105	2070.9	2373.7	2569.1
		Mean	2071.4	2359.3	2509.2
		S.D.	58.8	57.7	84.5
G4	1000	1401	2047.5	2189.9	2237.8
		1402	2098.6	2183.5	2377.2
		1403	2078.3	2369.9	2543.8
		1404	2102.8	2376.3	2475.1
		1405	2100.6	2352.2	2452.7
		Mean	2085.6	2294.4	2417.3
		S.D.	23.4	98.7	116.6

S.D. : Standard deviation

Appendix 4. Body weight of female rabbits

unit : g

Group	Dose (mg/kg)	No.	Days after administration		
			0	7	14
G1	0	2101	2296.2	2527.6	2712.7
		2102	2200.2	2528.4	2599.5
		2103	2159.5	2463.7	2528.8
		2104	2047.1	2293.0	2629.2
		2105	2069.6	2302.1	2473.2
		Mean	2154.5	2423.0	2588.7
		S.D.	101.2	117.5	92.3
G2	250	2201	2086.3	2399.3	2615.2
		2202	2126.6	2395.7	2535.3
		2203	2123.2	2354.0	2405.7
		2204	2097.0	2423.6	2679.9
		2205	2097.8	2374.1	2604.6
		Mean	2106.2	2389.3	2568.1
		S.D.	17.7	26.4	104.3
G3	500	2301	2166.1	2357.7	2696.1
		2302	2062.2	2345.3	2522.5
		2303	2047.6	2244.2	2359.1
		2304	2096.0	2309.8	2539.8
		2105	2115.0	2412.0	2619.7
		Mean	2097.4	2333.8	2547.4
		S.D.	46.8	62.1	126.0
G4	1000	2401	2097.4	2310.3	2487.7
		2402	2139.2	2242.2	2431.2
		2403	2036.1	2207.5	2306.6
		2404	2278.7	2617.9	2819.2
		2405	2094.5	2365.6	2521.7
		Mean	2129.2	2348.7	2513.3
		S.D.	91.3	162.4	189.6

S.D. : Standard deviation

Appendix 5. Necropsy findings of male rabbits

Animal No.	1101	Group : G1	Dose :	0	mg/kg	Terminal sacrifice	: Day 14
Gross findings : No gross findings							
Animal No.	1102	Group : G1	Dose :	0	mg/kg	Terminal sacrifice	: Day 14
Gross findings : No gross findings							
Animal No.	1103	Group : G1	Dose :	0	mg/kg	Terminal sacrifice	: Day 14
Gross findings : No gross findings							
Animal No.	1104	Group : G1	Dose :	0	mg/kg	Terminal sacrifice	: Day 14
Gross findings : No gross findings							
Animal No.	1105	Group : G1	Dose :	0	mg/kg	Terminal sacrifice	: Day 14
Gross findings : No gross findings							
Animal No.	1201	Group : G2	Dose :	250	mg/kg	Terminal sacrifice	: Day 14
Gross findings : No gross findings							
Animal No.	1202	Group : G2	Dose :	250	mg/kg	Terminal sacrifice	: Day 14
Gross findings : No gross findings							
Animal No.	1203	Group : G2	Dose :	250	mg/kg	Terminal sacrifice	: Day 14
Gross findings : No gross findings							
Animal No.	1204	Group : G2	Dose :	250	mg/kg	Terminal sacrifice	: Day 14
Gross findings : No gross findings							
Animal No.	1205	Group : G2	Dose :	250	mg/kg	Terminal sacrifice	: Day 14
Gross findings : No gross findings							

Appendix 5. (Continued) Necropsy findings of male rabbits

Animal No.	1301	Group : G3 Dose : 500	mg/kg	Terminal sacrifice	: Day 14
Gross findings : Crust formation of administration site					
Animal No.	1302	Group : G3 Dose : 500	mg/kg	Terminal sacrifice	: Day 14
Gross findings : Crust formation of administration site					
Animal No.	1303	Group : G3 Dose : 500	mg/kg	Terminal sacrifice	: Day 14
Gross findings : Crust formation of administration site					
Animal No.	1304	Group : G3 Dose : 500	mg/kg	Terminal sacrifice	: Day 14
Gross findings : Crust formation of administration site					
Animal No.	1305	Group : G3 Dose : 500	mg/kg	Terminal sacrifice	: Day 14
Gross findings : Crust formation of administration site					
Animal No.	1401	Group : G4 Dose : 1000	mg/kg	Terminal sacrifice	: Day 14
Gross findings : Crust formation of administration site					
Animal No.	1402	Group : G4 Dose : 1000	mg/kg	Terminal sacrifice	: Day 14
Gross findings : Crust formation of administration site					
Animal No.	1403	Group : G4 Dose : 1000	mg/kg	Terminal sacrifice	: Day 14
Gross findings : Crust formation of administration site					
Animal No.	1404	Group : G4 Dose : 1000	mg/kg	Terminal sacrifice	: Day 14
Gross findings : Crust formation of administration site					
Animal No.	1405	Group : G4 Dose : 1000	mg/kg	Terminal sacrifice	: Day 14
Gross findings : Crust formation of administration site					

(End)

Appendix 6. Necropsy findings of female rabbits

Animal No.	2101	Group : G1	Dose :	0	mg/kg	Terminal sacrifice	: Day 14
Gross findings : No gross findings							
Animal No.	2102	Group : G1	Dose :	0	mg/kg	Terminal sacrifice	: Day 14
Gross findings : No gross findings							
Animal No.	2103	Group : G1	Dose :	0	mg/kg	Terminal sacrifice	: Day 14
Gross findings : No gross findings							
Animal No.	2104	Group : G1	Dose :	0	mg/kg	Terminal sacrifice	: Day 14
Gross findings : No gross findings							
Animal No.	2105	Group : G1	Dose :	0	mg/kg	Terminal sacrifice	: Day 14
Gross findings : No gross findings							
Animal No.	2201	Group : G2	Dose :	250	mg/kg	Terminal sacrifice	: Day 14
Gross findings : No gross findings							
Animal No.	2202	Group : G2	Dose :	250	mg/kg	Terminal sacrifice	: Day 14
Gross findings : No gross findings							
Animal No.	2203	Group : G2	Dose :	250	mg/kg	Terminal sacrifice	: Day 14
Gross findings : No gross findings							
Animal No.	2204	Group : G2	Dose :	250	mg/kg	Terminal sacrifice	: Day 14
Gross findings : No gross findings							
Animal No.	2205	Group : G2	Dose :	250	mg/kg	Terminal sacrifice	: Day 14
Gross findings : No gross findings							

Appendix 6. (Continued) Necropsy findings of female rabbits

Animal No.	2301	Group : G3	Dose :	500	mg/kg	Terminal sacrifice	: Day 14
Gross findings : Crust formation of administration site							
Animal No.	2302	Group : G3	Dose :	500	mg/kg	Terminal sacrifice	: Day 14
Gross findings : Crust formation of administration site							
Animal No.	2303	Group : G3	Dose :	500	mg/kg	Terminal sacrifice	: Day 14
Gross findings : Crust formation of administration site							
Animal No.	2304	Group : G3	Dose :	500	mg/kg	Terminal sacrifice	: Day 14
Gross findings : Crust formation of administration site							
Animal No.	2305	Group : G3	Dose :	500	mg/kg	Terminal sacrifice	: Day 14
Gross findings : Crust formation of administration site							
Animal No.	2401	Group : G4	Dose :	1000	mg/kg	Terminal sacrifice	: Day 14
Gross findings : Crust formation of administration site							
Animal No.	2402	Group : G4	Dose :	1000	mg/kg	Terminal sacrifice	: Day 14
Gross findings : Crust formation of administration site							
Animal No.	2403	Group : G4	Dose :	1000	mg/kg	Terminal sacrifice	: Day 14
Gross findings : Crust formation of administration site							
Animal No.	2404	Group : G4	Dose :	1000	mg/kg	Terminal sacrifice	: Day 14
Gross findings : Crust formation of administration site							
Animal No.	2405	Group : G4	Dose :	1000	mg/kg	Terminal sacrifice	: Day 14
Gross findings : Crust formation of administration site							

(End)

11. Annexes

Annex 1. Information of test substance (Submitted by sponsor)

Substance Data Sheet

Date : 2012.06.26 (yr/m/d)		Corresponding person	Fine Fisher (署名)
試験物質 (Test article)			
試験物質名* (Test article name)	AMDS	供給元* (Supplier)	Sim Fine Mark Sz
製造日* (Manufacturing date)	2012.06.26. (yr/m/d)	運送方法* (Delivery method)	☐Mail ☒Express ☐Self ☐Etc. ( ) 実重量(Net)
運送条件* (Delivery condition)	☐室温(1~30℃) ☐常温(15~25℃) ☐冷蔵(2~8℃) ☐冷凍(-15~-25℃) ☐その他( )	提供量* (Delivery amount)	( ) (☐g ☐ml) 容器含む(Gross) (526) (☐g ☒ml)
Cas No.*	(999-97-3)	ロット番号* (LOT No.)	(120100)
試験期間中保管条件* (Storage condition)	☐室温(1~30℃) ☐常温(15~25℃) ☐冷蔵(2~8℃) ☐冷凍(-15~-25℃) ☐Etc.( )	有効期間* (Expiration date)	20 (yr/m/d) n/a (製造後 ヵ月)
外観及び性状* (Physical description)	Liquid Solvent	純度* (Purity)	(>99 %)
分子式(分子量) (Molecular formular(M.W))	( )	比重 (Specific gravity)	1.0
Partition Coefficient(K_{ow})	Likely	水溶解度 (Solubility in water)	Not Soluble
残留試験物質処理方法 (Treatment after End of study)*	☐Return ☒Disposal	取扱/廃棄時注意事項* (Caution in handling or disposal)	Reference SDS
発送(予定)日* (Delivery date)	2012.06.26 (yr/m/d) Estimate	発送者* (Sender)	Chi Fine Mark (株)
試験物質調剤 (Formulation)			
媒体/溶解性* (Vehicle control and solubility)	☐WFI ☐Saline ☐DMSO ☐DMF ☐Vaseline ☐エタノール ☐アセトン ☐Veg. Oil(Corn oil Olive oil) ☐( )% CMC ☐( )% MC ☐Etc.( )	保管条件* (Storage condition)	☐室温(1~30℃) ☐常温(15~25℃) ☐冷蔵(2~8℃) ☐冷凍(-15~-25℃) ☐Etc
安定性 (Stability)	( )	均質性 (Homogeneity)	
臨床予定経路 (Route of clinic)	☐Oral ☒Dermal ☐Vein ☐Etc ( )	臨床予定容量 (Dose conc. of clinic)	☐ (mg/kg/BW) ☐ (mg/kg/BSA)
調剤方法及び注意事項* (Preparation method and Caution)	☐Pind attached ☒Other ☐Etc ( )		
添付資料* (Attachment)	☒試験物質成績書(Certificate of Analysis) ☒MSDS ☐Stability report ☐Efficacy report ☒Toxic test report ☐Other report ☐Reference ☐Preparation method ☒Analytical method ☐Standard ☐Etc ( )		

備考* (Remark)	NONE

Annex 2. Certificate of analysis (Submitted by sponsor)

Shin-EtsuMicroSi

10026 S. 51st St., Phoenix, AZ 85044 Ph: (480) 893-8898, Fax: (480) 893-8637

Certificate of Analysis
Microprime HP Primer

Shin-Etsu MicroSi Product Number	MPHP
Lot Number	1201006
Date of Manufacture	6/18/2012
Date of Expiration	12/10/2013

ANALYSIS

Item	Specification	Results
Formulation Purity (%)	99.7 % min.	99.8
Trailing Impurities (%)	0.1% max	< 0.1
Color (APHA)	10 max	10
Residue (ppm)	10.0 max.	0.5
UV Absorbance @ 270nm	0.25 max.	0.06
Specific Gravity	0.768 +/- 0.004	0.768
Refractive Index @ 25°C	1.4050 +/- 0.0010	1.4059
Turbidity (NTU)	1.0 max	< 0.5
Chloride (ppm)	0.3 max.	< 0.1
Particles ≥ 0.5 µm	< 50 counts/ml	5
Water content	< 50ppm	9

Trace Metals Analysis (ppb)					
Al (10 max.)	0.3	Ga (10 max.)	< 0.05	Na (10 max.)	0.5
Sb (10 max.)	< 0.1	Ge (10 max.)	< 0.1	Pt (10 max.)	< 1
As (10 max.)	< 0.2	Au (10 max.)	< 1	Sr (10 max.)	< 0.05
Ba (10 max.)	< 0.05	Fe (10 max.)	< 0.5	Ta (10 max.)	< 0.1
Be (10 max.)	< 0.1	Pb (10 max.)	< 0.1	Ti (10 max.)	< 0.2
Bi (10 max.)	< 1	Li (10 max.)	< 0.05	Sn (10 max.)	< 1
B (10 max.)	< 1	Mg (10 max.)	0.6	Ti (10 max.)	< 1
Cd (10 max.)	< 0.1	Mn (10 max.)	< 0.1	V (10 max.)	< 0.1
Ca (10 max.)	2.6	Mo (10 max.)	< 0.1	Zn (10 max.)	< 0.5
Cr (10 max.)	< 0.5	Ni (10 max.)	< 0.1	Zr (10 max.)	< 0.1
Co (10 max.)	< 0.05	K (10 max.)	< 0.5		
Cu (10 max.)	< 0.5	Ag (10 max.)	< 1		

Certified By:

Name: *James McElwania*
Quality Control Department
Date: June 18, 2012

Annex 3. Amendment document of study plan

Amendments of study plan

Study title	Acute dermal toxicity study of HMDS in NZW rabbit	Study number	TBH-1166 (KG-2012-384)
Study period	2012-09-12 ~ 2012-10-31		

Amendments and Reason for amendment

〈 Amendment 〉

- Information for Management
  1) Before : Park Gil-jong
  2) After : Kim Ki-sung

〈 Reason 〉

- Change in personnel (Personnel order No. 47, 2012-09-11)
- Management change in GLP Certificate
  (National Institute of Environmental Research, Certification No. 2008-6)
  (2012-09-21)

Study director	: Shin Sung-Sup	Sponsor	: [illegible]
Date (yr/m/d)	: 2012-09-28	Date (yr/m/d)	: 10/1/2012
QAU	: Park Jong Il	Date (yr/m/d)	: 2012-09-28
Management	: Ki Sung Kim	Date (yr/m/d)	: 2012-09-28

ShinEtsuMicroSi®

MICROELECTRONIC MATERIALS

10028 S. 51st Street • Phoenix, AZ 85044

U.S. POSTAGE
PAID
PHOENIX,AZ
85048
FEB 06, '13
AMOUNT

$7.57
00049140-06

CERTIFIED MAIL™

7008 1830 0000 0757 7452