TEST REPORT

STUDY REPORT NUMBER: MB-PSI-03-E-16-10-A1

(Replacement to study report number MB-PSI-03-E-16-10)

Study Completion Date: 09 NOV 2010

Title: PRIMARY SKIN IRRITATION

Sky Gel (Ultrasound Gel)

Study Sponsor	**Testing Facility**
ISD Meditech Sdn Bhd No. 12, Jalan Teras1, Taman Industri Teras, 43300, Balakong, Selangor.	**Makmal Bioserasi** INBIOSIS Universiti Kebangsaan Malaysia 43600 UKM Bangi Selangor Malaysia.

Study Director : Assoc Prof Dr Md Anuar Osman

Quality Assurance Personnel : Nur Nadiah Yusoff

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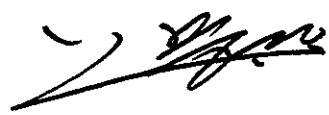
- This report contains 15 pages.
- This test report concerns only the product being tested.

Primary Skin Irritation Test

Study Director	**Signature**
Assoc. Prof. Dr. Md. Anuar Osman *DVM (Pak), M. Sc (W. Aust), Ph.D (Murdoch)*	 **Date:** 9/11/10
Sponsor	**Signature**
ISD Meditech Sdn Bhd ISD MEDITECH SDN BHD (915725-T) NO. 12, JALAN TERAS 1, TAMAN INDUSTRI TERAS 43300 BALAKONG, SELANGOR TEL 03-89616880 FAX 03-89619880	 **Date:** 15/11/2010

TEST REPORT - Primary Skin Irritation Test

TABLE OF CONTENTS		**PAGE**
SUMMARY		3
TEST REPORT		
1.	Sponsor of Test Material	5
2.	Details of Test Material	5
3.	Laboratory Facility	5
4.	Test Method	8
5.	Number of Test Material Replicate	10
6.	Controls	10
7.	Quality Assurance	11
8.	Deviations from Approved Protocol	11
9.	Records to be Maintained	11
10.	Dates of Test Procedures	11
11.	Summary of Results	11
12.	Interpretation of Results	13
13.	Conclusions	13
14.	References	13
15.	Verification	14
16.	Quality Assurance Inspections Statement	15

SUMMARY

Primary Skin Irritation Test

Protocol reference : PR-PSI-03

Method used : ISO 10993-10:2002 (E)

Study completion date : 9 Nov 2010

Study reference number : PSI-03-01-10

Study report number : MB-PSI-03-E-16-10-A1
(Replacement to study report number MB-PSI-03-E-16-10)

Job number : E-16-10

Test material : Sky Gel (Ultrasound Gel)

Conditions of use : Neat

1. OBJECTIVE

To provide information on the irritation effects likely to arise from a single 24-hour exposure of test material on intact skin of rabbits.

2. EXPERIMENTAL PROCEDURE

Animals: Three New Zealand white rabbits weighing 2.19 kg to 2.92 kg.

Acclimatization period	27 April – 4 May 2010
Date of initiation	4 May 2010
Dates of observation	4 May – 8 May 2010
End of test	8 May 2010

Treatment

Test material (Sky Gel (Ultrasound Gel)) was applied on a filter paper and placed in direct contact with the intact skin of each rabbit. Two additional sites which were identified for positive control (SDS in petroleum jelly) and negative control (normal saline) were individually placed in contact with the skin under a patch of gauze and occlusive material for 24 hours.

3. OBSERVATIONS

Cutaneous macroscopical examinations were performed at 1 hour, 24 hours, 48 hours and 72 hours after removal of test material. Evaluations of the erythematous and oedematous lesions were performed according to the classification established by the ISO 10993-10:2002(E). Biological evaluation of medical devices – Part 10: Tests for irritation and delayed-type hypersensitivity.

TEST REPORT

1.0 SPONSOR OF TEST MATERIAL

1.1	**Name**	: ISD Meditech Sdn Bhd
1.2	**Address**	: No. 12, Jalan Teras 1, Taman Industri Teras, 43300 Balakong, Selangor.
1.3	**Study report number**	: MB-PSI-03-E-16-10-A1 *(Replacement to study report number MB-PSI-03-E-16-10)*
1.4	**Job number**	: E-16-10

2.0 DETAILS OF TEST MATERIAL

2.1	**Name**	: Sky Gel (Ultrasound Gel)
2.2	**Intended use of test material**	: Ultrasound Screening Procedure
2.3	**Test material reference**	: MD16-E0410
2.4	**Study reference number**	: PSI-03-01-10
2.5	**Lot number**	: N/A
2.6	**Date test material received**	: 16 April 2010
2.7	**Expiry date**	: N/A
2.8	**Appearance**	: Gel
2.9	**Colour**	: Blue
2.10	**Quantity**	: 2 packets
2.11	**Storage**	: Refrigerated
2.12	**Solubility**	: Water
2.13	**Condition of use**	: Neat
2.14	**Dates of study**	: 4 May to 8 May 2010
2.15	**End of test**	: 8 May 2010
2.16	**pH**	: N/A

3.0 LABORATORY FACILITY

3.1	**Name**	: Makmal Bioserasi
3.2	**Address**	: INBIOSIS, Universiti Kebangsaan Malaysia, 43600 UKM, Bangi, Selangor, Malaysia.

3.5 Study timetable

3.5.1	Acclimatization period	27 April – 4 May 2010
	Date of initiation	4 May 2010
	Dates of observation	4 May – 8 May 2010
3.5.2	End of test	8 May 2010

3.6 Authorization

Approval from Universiti Kebangsaan Malaysia Animal Ethics Committee (UKMAEC) for study entitled: Safety assessment of cosmetics, topical traditional preparations, plastics, gloves, rubber fibres and medical devices (Animal study).

3.7 Environment and husbandry

3.7.1 Species and strain
New Zealand white rabbits.

3.7.2 Supplier
Animal Breeding Facility of the Faculty of Science and Technology, Universiti Kebangsaan Malaysia, Bangi, Selangor.

3.7.3 Number of animal and sex
Three (All females).

3.7.4 Body weight at initiation of study
Minimum: 2.19 kg; Maximum: 2.92 kg.

3.7.5 Age
Young Adult.

3.7.6 Housing
Animals were housed individually in suspended stainless steel cages with mesh floors of internal dimension: 40 cm by 40 cm by 60 cm. Rabbits were selected randomly prior to acclimatization.

3.7.6.1 Animal room temperature
22 ^{0}C to 25 ^{0}C.

3.7.6.2 Photoperiod
Twelve-hour light/dark cycle.

3.7.6.3 Acclimatization period
Seven days.

3.7.7 Diet
Standard rabbit pellet

3.7.8 Water
Pre-filtered tap water *ad libitum* continuously supplied in water dispensing bottles.

4.4 Description of test procedure

4.4.1 The dorsal area of three healthy New Zealand white rabbits were clipped free of hair at least 4 hours prior to the initiation of the study. Care was taken to avoid abrading the skin.

4.4.2 Each rabbit was housed in a separate cage and assigned specific numbers from 1 to 3.

4.4.3 For each rabbit, the skin was tested with 2.5 cm by 2.5 cm filter paper layered with 0.5 ml test material in one area and with a negative control in the other. Another designated test site was also tested with positive control.

4.4.4 All three rabbits were tested with the skin contact surface of the test material. Each of the test material and the controls was then individually covered with a double layered surgical gauze. The gauze pad and the entire trunk of each animal was then covered and wrapped with a non-reactive adhesive tape to minimize evaporation and to avoid dislocation of the gauze pad. After the entire test sites were again wrapped with an elastic bandage * the rabbits were returned to their individual cages.

4.4.5 After 24 hours of exposure to the test material, the patches and rubberized cloth were removed and the test sites were gently wiped with a moist clean towel to remove any residual test material. Individual dose sites were scored according to the scoring system for skin reaction at 1 hour, 24 hours, 48 hours and 72 hours after removal of test material (see Table 1).

4.4.6 Animals were examined once daily. These observations were reported in the study raw data documents. Autopsy was not recommended for live animals.

4.4.7 Cage-side observations
Animals were observed for signs of gross toxicity and behavioral changes at least once daily during the test period. Observations included gross evaluation of skin and fur, eyes and mucous membranes, respiratory, circulatory, autonomic and central nervous systems, somatomotor activity and behavior pattern. Particular attention was also directed to signs of tremors, convulsions, salivation, diarrhea and coma.

* Aids in maintaining the test patches in position.

7.0 QUALITY ASSURANCE

The final report was audited in agreement with the raw data records and for compliance with the protocols and Standard Operating Procedures of Makmal Bioserasi. Dates of inspection and audit performed during the study and the dates of reporting of the inspection and audit findings to the Study Director are presented in the Quality Assurance Statement.

8.0 DEVIATIONS FROM APPROVED PROTOCOL

None.

9.0 RECORDS TO BE MAINTAINED

A copy of this signed report together with the protocol and all raw data generated at the laboratory are retained in Makmal Bioserasi archive.

10.0 DATES OF TEST PROCEDURES

Acclimatization period	27 April – 4 May 2010
Date of initiation	4 May 2010
Dates of observation	4 May – 8 May 2010
End of test	8 May 2010

11.0 SUMMARY OF RESULTS

11.1 Treatment

Test Material : Sky Gel (Ultrasound Gel)
Study reference number: PSI-03-01-10

Table 2a: Scoring of cutaneous reaction for test material: Sky Gel (Ultrasound Gel) (For scoring please refer to Table 1).

No	Animal Number / Sex	Readings at 1 hour (Post removal)		Readings at 24 hours (Post removal)		Readings at 48 hours (Post removal)		Readings at 72 hours (Post removal)		Primary Irritation Score (Mean)
		Score		Score		Score		Score		
		Erythema	Oedema	Erythema	Oedema	Erythema	Oedema	Erythema	Oedema	
1	r045a Female	0	0	0	0	0	0	0	0	0
2	r053a Female	0	0	0	0	0	0	0	0	0
3	r054a Female	0	0	0	0	0	0	0	0	0

12.0 INTERPRETATION OF RESULTS

Table 3: Primary Irritation Index of test material group, negative control group and positive control group.

	Primary Irritation Score (Mean)		
Animal Number	**Test Material**	**Negative Control (Normal saline)**	**Positive Control (SDS in petroleum jelly)**
r045	0	0	8.00
r053	0	0	7.33
r054	0	0	4.33
Primary Irritation Index	**0**	**0**	**6.55**

All three animals appeared active and healthy. There were no signs of gross toxicity, adverse pharmacological effects, and abnormal behaviour observed. No irreversible alterations on the skin at the site of contact with test material were found. There was no erythema or oedema noted on the test sites after 24 hours and 72 hours. The Primary Irritation Index (PII) was '0'.

Cutaneous reactions at the site of contact with positive control (SDS in petroleum jelly) was observed with evidence of erythema and oedema noted on most test sites after 24 hours and 72 hours. The Primary Irritation Index (PII) was '6.55'.

13.0 CONCLUSIONS

The Primary Skin Irritation Index (PSII) of the test material was '0'. The test material, **Sky Gel (Ultrasound Gel)** was not corrosive and the Primary Irritation Response Category is therefore 'Negligible'.

14.0 REFERENCES

1. ISO 10993-10:2002(E). Biological evaluation of medical devices – Part 10: Tests for irritation and delayed-type hypersensitivity.
2. ISO 10993-12:2007(E). Biological evaluation of medical devices – Part 12: Sample preparation and reference materials.
3. Medical Glove Guidance Manual
4. Consumer Product Safety Commission, Title 16, Chapter II, Part 1500.

15.0 VERIFICATION

I the undersigned declare that the methods, results and data contained in this report faithfully reflect the procedures used and the raw data collected during the course of study.

Assoc. Prof. Dr Md. Anuar Osman
Study Director

9/11/10
Date

16.0 QUALITY ASSURANCE INSPECTIONS STATEMENT

This study has been inspected by the Quality Assurance Personnel, and the findings have been reported to Study Director on the following dates:

Procedures Inspected	Inspected Dates	Reported Dates
a. Patch application	4 May 2010	18 May 2010
b. Scoring after patch removal	5 May 2010	18 May 2010
c. Records and Report	18 May 2010	18 May 2010

b/p: Dana

Nur Nadiah Yusoff
Quality Assurance Personnel

9 Nov 2010
Date

4.5 Scoring method

The appearance of each application site at 1 hour, 24 hours, 48 hours and 72 hours following removal of the patches were recorded and scored as in Table 1a below.

Table 1a: Scoring system for skin reaction.

Reactions	Description	Score
Erythema (E)	Erythema and eschar formation	
	No erythema	0
	Very slight erythema (barely perceptible)	1
	Well-defined erythema (pale red in colour)	2
	Moderate erythema (red and area well-defined)	3
	Severe erythema (beet redness) to eschar formation preventing grading of erythema	4
Oedema (O)	Oedema formation	
	No oedema	0
	Very slight oedema (barely perceptible)	1
	Well-defined oedema (edges of the area well defined by definite raising)	2
	Moderate oedema (raised approximately 1mm)	3
	Severe oedema (raised more than 1mm and extending beyond exposure area)	4
Total possible score for irritation		8
Other adverse changes at the skin sites shall be recorded and reported		

4.6 Interpretation of Results

Only observations at 24 hours, 48 hours and 72 hours were used for calculations. The Primary Irritation scores for the test material for both erythema and oedema at each time point for each animal were combined and the summation of the combined scores was divided by the total number of observations. The Primary Irritation Score is obtained by subtracting the Primary Irritation Score of control from the Primary Irritation Score of test material. The scores for each animal were added together and divided by the total number of animals. This value is the Primary Irritation Index. The Primary Irritation Index is characterised by number (score) and description (response category) tabulated in Table 1b.

Table 1b: Irritation Response categories in rabbit

Mean score	Response category
0 to 0.4	Negligible
0.5 to 1.9	Slight
2 to 4.9	Moderate
5 to 8	Severe

5.0 NUMBER OF TEST MATERIAL REPLICATE

Three sets.

6.0 CONTROLS

Normal saline as negative control and SDS in petroleum jelly was used as positive control.

3.8 Pre-Treatment procedures

3.8.1 Check for ill health

On arrival and just before the beginning of treatment to ensure only healthy animals were used in the study. Rabbits showing cutaneous lesions that would interfere with the study were not included.

3.8.2 Body weight

All animals were weighed just before treatment.

3.8.3 Identification

Cages : Labeled with animal number, sex and job number.

Animal : Each rabbit was marked with animal identification on the inner side of the ear using marker pen.

3.8.4 Preparation of the skin

The dorsal area of each side of the rabbit was clipped free of hair with the help of a clipper to expose a surface of about 10 cm by 15 cm. Care was taken to avoid abrading the skin. After clipping and prior to initiation, animals were examined for any abnormalities and ill health. Only animals without pre-existing skin irritation were selected for the study. On each rabbit, three test sites were delineated, one site for test material and one site for negative control. An additional test site was also identified for positive control.

4.0 TEST METHOD

4.1 Name of test: Primary Skin Irritation Test [1,2]

4.2 Objective

To study the primary irritation effect of test material (Sky Gel (Ultrasound Gel)) on the skin of rabbits.

4.3 Materials

4.3.1 Test system

Three healthy New Zealand white rabbits, all females.
Weight: 2.19 kg to 2.92 kg.

4.3.2 Auxiliary materials

Double layered surgical gauze.
Non-reactive adhesive tape.
Elastic bandage.

4.3.3 Test conditions

The test material was applied on a filter paper and placed on the test site. Absorbent gauze (2.5 cm by 2.5 cm) soaked in normal saline was used as negative control. SDS in petroleum jelly was identified for positive control.

4.3.4 Test material preparation

The test material was applied neat.

3.3 Project staff

3.3.1 Study Director
Assoc. Prof. Dr. Md. Anuar Osman
DVM (Pak), M. Sc (W. Aust), PhD (Murdoch)

3.3.2 Study Personnel
Mimi Norhilda Binti Mohd Hatta
Mohd Hisyam Syabril Bin Yaacob

3.3.3 Quality Assurance Personnel
Nur Nadiah Bt Yusoff

3.4 Address of correspondence

Makmal Bioserasi, Institut Biologi sistem (INBIOSIS)
Universiti Kebangsaan Malaysia,
43600 UKM, Bangi,
Selangor, Malaysia.
Fax: 03-89214281
Tel: 03-89214280

c/o
Assoc. Prof. Dr. Md. Anuar Osman

4. RESULTS

All three animals appeared active and healthy. There were no signs of gross toxicity, adverse pharmacological effects, and abnormal behaviour observed. No irreversible alterations on the skin at the site of contact with test material were found. There was no erythema or oedema noted on the test sites after 24 hours and 72 hours. The Primary Irritation Index (PII) was '0'.

Cutaneous reactions at the site of contact with positive control (SDS in petroleum jelly) was observed with evidence of erythema and oedema noted on most test sites after 24 hours and 72 hours. The Primary Irritation Index (PII) was '6.55.

5. CONCLUSION

The Primary Skin Irritation Index (PSII) of the test material was '0'. The test material, **Sky Gel (Ultrasound Gel)** was not corrosive and the Primary Irritation Response Category is therefore 'Negligible'.