Coronati lab

Consulenza e Servizi di Laboratorio per la Qualità Biomedicale

CUTANEOUS IRRITATION TEST

"Soletta con lamina in lega"

According to UNI EN ISO 10993-10

REPORT N. 148-12

Customer: MACROLAB S.r.l. per conto di MEDIKA s.r.l.

Via Lea Cazzuoli, 15 - 41037 Mirandola (MO)

TIME SCHEDULE

Acceptance N:	11-3179
Samples receiving date:	07/12/11
Start test date:	14/12/11
End test date:	23/12/11

TEST LABORATORY

Coronati Consulting sas Via G. Gavioli, 3 I-41037 Mirandola (MO)

The test has been commissioned to:
Eurofins Biolab S.r.l. (MI) Italy

Mirandola	Prepared by: Dr.C.Pellegrini	Verified and Approved by: Dr. R. Coronati
26/01/2012		

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REFERENCE DOCUMENTS

- UNI EN ISO 10993-1: 2010 Biological evaluation of medical devices– Evaluations and testing
- UNI EN ISO 10993-2: 2006 Animal welfare requirements
- UNI EN ISO 10993-10: 2010 Tests for irritation and sensitization
- UNI EN ISO 10993-12: 2009 Samples and reference materials

SAMPLE

Sample:	Soletta con lamina in lega
Qty tested:	10
Code (REF):	Taglia 40
Art:	NA
Lot:	Campione 2011
Manufacture date:	n.d.
Expiry date:	n.d.
Sterilization Method:	NA
Sterilization lot:	NA

PROCEDURE

Animal

For the test were used three white Rabbit, New Zeland, weight 3460-4000 g at the beginning of the test.
Supplier: Allevamento Bettinardi. Momo-(No) Italy

Caging

Each rabbit was caged in stainless steel cages of cm 45×50×38h equipped with automatic washing cycle.
The housing room was lighted with fluorescent lamps 12 hours for day.
Room temperature and humidity were regulated by a conditioning plant and were monitored daily.
Recordings of the housing conditions are being retained in Eurofins Biolab srl files.

Cleaning and disinfection

The cages and the housing room were cleaned before the animals were accommodated, then disinfected periodically. The cages were provided with automatic washing equipment.

Feeding

Animals have been fed with standard pellet complete diet supplied by the authorised breeder Harlan.

Watering

Filtered tap water from local network was supplied ad libitum .

Animal Identification

A numbered plastic tag placed through the edge of the right ear identified the animals selected for the study.
A label identified the cages.

Quarantine

Before allocation to the study, the animals were kept in quarantine for five days. During this period they were observed daily.
At the end of the quarantine week the animals were carefully examined in order to evaluate their suitability for the study.

Animal selection

The animals used for this study were selected randomly from those suitable, available at that time.

PREPARATION FOR THE ASSAY STUDY

The test product has been used neat .

EXPERIMENTAL DESIGN

Three male white rabbits were used.
Each animal had the right caudal region and left cranial region treated with the test product.
The right cranial region and the left caudal region was treated with a no irritant gauze (25mm×25mm) humidified with physiological solution, used as control. The reactions could be present in the treated area were compared with those of the control area.

Treatment

Skin preparation

Approximately 24 hours before the test, the fur was removed from an area approximately 240cm2 wide by clipping and shaving the dorsal and flank zones of the animals.
An area of the back, about 6 cm2 wide, was designed for the application of the test sample.

Application

25×25 mm of the test product were applied with a gauze (25mm×25 mm) directly to the skin on the dorsum of each rabbit after humidification with sodium chloride injection and covered with non-occlusive dressing, than the trunk was protected with a semi-occlusive bandage.

Removal of the patches

The patches were removed 4 hours after the application.

OBSERVATIONS

General conditions of the animals were verified daily. Reactions were evaluated following the removal of the patches and were evaluated again at 24, 48 and 72 hours after exposure.
Skin irritation was scored and recorded according to the scores reported in the following table.

Scoring system

The score system assigned to each site is reported below.

SCORING SYSTEM FOR CUTANEOUS IRRITATION			
Erythema and Eschar / Excoriations	**Score**	**Oedema**	**Score**
No erythema	0	No oedema	0
Discrete o pacthy erythema, barely perceptible	1	Oedema barely perceptible	1
Moderate and confluent erythema	2	Well-defined Oedema	2
Intense erythema and swelling	3	Oedema moderate (in relief of 1 mm)	3
Erythema severe red beet type to eschar formation	4	Oedema serious in relief > 1 mm and extended	4
Possible total irritation score: 8			
Note: other adverse changes of the injection sites must be recorded and reported			

INTERPRETATION OF THE RESULTS

For acute exposure, determine the Primary Irritation Index as follows
For each animal, add together the Primary Irritation scores for the test substance for both erythema and edema at each time specified and divide by the total number of observations. When vehicle controls and subtract that score from the score for the test substance to obtain the Primary irritation Score.
Only use 24 hours and 72 hours observations for calculations.
Observation made prior to dosing or after 72 hours to monitor recovery are not used in the determination.
Add the scores for each animal and divide the total number of animals. This value is the Primary Irritation index.
Number and description in follow table characterise the Primary Irritation index:

Score	Response
0,0 ÷ 0,4	Negligible
0,5 ÷ 1,9	Slight irritation
2,0 ÷ 4,9	Moderate irritation
5,0 ÷ 8,0	Severe irritation

RESULTS

The values of skin reactions at different observation periods for individual rabbits are shown in the table below.

Reaction	Time	Rabbit n. 1				Rabbit n.2				Rabbit n. 3			
		Treated area		Not treated area		Treated area		Not treated area		Treated area		Not treated area	
		SX	DX	SX	DX	SX	DX	SX	DX	SX	DX	SX	DX
Eritema	60 min	0	0	0	0	0	0	0	0	0	0	0	0
	24 h	0	0	0	0	0	0	0	0	0	0	0	0
	48 h	0	0	0	0	0	0	0	0	0	0	0	0
	72 h	0	0	0	0	0	0	0	0	0	0	0	0
Edema	60 min	0	0	0	0	0	0	0	0	0	0	0	0
	24 h	0	0	0	0	0	0	0	0	0	0	0	0
	48 h	0	0	0	0	0	0	0	0	0	0	0	0
	72 h	0	0	0	0	0	0	0	0	0	0	0	0

In region treated with the test sample no oedema or erythema have been observed.
In treated and control regions no oedema or erythema have been observed.

Primary skin irritation Index of the test substance: 0,00
Primary skin irritation Index of control: 0,00
PRIMARY SKIN IRRITATION INDEX: 0,00

DEVIATION: No deviation has been recorded from study program.

CONCLUSIONS

On the basis of the results, interpreted according to ISO 10993-10: 2010, the test product must be considered NOT IRRITANT for the skin.

⇒ The present test report refers only to the samples examined.