ISO 10993-10:2014
Skin Sensitization Test

Company Name Firma Adı	**AVAS KOZMETİK SANAYİ VE TİCARET LİMİTED ŞİRKETİ**
Company Address Firma Adresi	**GÖKEVLER MAH. 2331 SK. PASİAD NO. 1 D ESENYURT - İSTANBUL / TÜRKİYE**
Test Name Testin Adı	**Skin Sensitization Test**
Test Standard Test Standardı	**TS EN ISO 10993-10:2014**
Commercial Brand (If You Have) Ticari Marka (Varsa)	**Felix Filler**
Description of the Sample Numunenin Adı ve Tarifi	**1 cc Felix Filler Dolgu**
Lot Number Lot Numarası	**AVAS012023-1**
Sample Registration Number Numune Kayıt Numarası	**FLXFHA/202302**
Sample Acceptance Date Numune Kabul Tarihi	**27.02.2023**
Report Number Rapor Numarası	**2023-03/BIYO/1532HA-DST**
Date of Report Rapor Tarihi	**10.03.2023**
Date of Test Deney Tarihi	**06.03.2023 - 09.03.2023**
Report Total Page Raporun Sayfa Sayısı	**9 Page /** ***Sayfa***

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SUMMARY

1 cc Felix Filler Dolgu sample number AVAS012023-1 has been subjected to biocompatibility testing according to TS EN ISO 10993-10 Biological evaluation of medical devices - Part 10: Tests for irritation and skin sensitivity. Samples were prepared by storing 37ºC-72 hours in SF under sterile conditions according to TS EN ISO 10993-12 Biological evaluation of medical devices - Part 12: Sample preparation and reference materials standard. The extract was intradermally injected into 10 guinea pigs. 5 experimental animals were used as a control group and previously determined Serum Physiological was injected. On day 7, after the completion of the intradermal induction phase, the superficial induction phase was applied to both the test group and the control group. On the 14th day after the induction phase, the stimulation phase was applied to the test group and the control group. The dressings and patches were removed after 24 hours. Necessary evaluations were made according to Magnusson and Kligman ratings at 24th and 48th hours. Under the terms of this study, **1 cc Felix Filler Dolgu extract showed no evidence of sensitization**.

1. INTRODUCTION

Purpose : This test was performed to evaluate the sensitivity of the sample described below to cause sensitivity.

Test Guide: This study was conducted according to the requirements of the International Organization for Standardization. 10993: Biological Assessment of Medical Devices, Part 10: Tests for Irritation and Skin Sensitivity

Dates

Sample Acceptance Date : 27.02.2023
Test Date : 06.03.2023
Observation Date : 06.03.2023 - 09.03.2023

2. SAMPLE INFORMATION

Company Name :	Avas Kozmetik
Date of the Sample Acceptance :	27.02.2023 13.05
Sample Record Number :	FLXFHA/202302
Sample Lot Number :	AVAS012023-1
Number of Sample :	4
Packaging Infirmation :	CLOSED PACKED
Sample Delivery Method :	CARGO
Expiration Date of the Sample :	17.01.2028
Production Date of the Sample :	17.01.2023
Description of the Sample :	Bir şırınga 1 cc Felix Filler dolgu maddesi içermektedir.
Characteristics of the Sample Use/Application :	Cross linked hyaluronic acid

Sample Image :

3. TEST SYSTEM

Animal used in the test :	Guinea Pig
Strain :	Dunkin Hartley
Source :	Burdur Mehmet Akif Ersoy University Experimental Animals Production and Research Center
Gender :	Male
Weight :	400 - 500 Gr
Age :	10 - 12 Week
Acclimation time :	5 Days
Number of the animals :	15

4. ANIMAL MANAGEMENT

Animal Care :	The animals used in the experiments are performed in accordance with the standards of Biological Evaluation of Medical Devices - Part 2: Requirements for Animal Welfare.
Food :	The SDS brand VRF1 diet is provided as ad-libitum.
Water :	Water is supplied as ad-libitum in suitable drinkers.
Cage System :	Each animal was identified and placed in appropriate cages.
Environmental Conditions :	12 hours night and 12 hours day environment is provided; 30-70% humidity and 16-22℃ environment is provided. Temperature and humidity are checked daily.
Personnel :	Tests are performed by trained and appropriately qualified personnel.
Selection of the animal :	Healthy, non-disease animals and non-pregnant animals were used under the supervision of a veterinary surgeon.
Veterinary Care :	This study was carried out under the supervision of a veterinarian.

5. METHOD

Sensitization tests; The Intradermal Inducing Phase was completed by observing the animals and evaluating the results after the Superficial Inducing Phase and Stimulation Phase.

In the Intradermal Inducing Phase; 0.1 ml intradermal applications were made with the following ingredients.

TEST GROUP:

Figure 1 Area A: Mixture of NOVAFIX ELASTIC FIXING TAPE A3294 -10 HX10 CM and FCA (Freund's Complete Adjuvant) at 50:50 volume ratio

Figure 1 Area B: Test Sample (Undiluted Extract) in Test Group

Figure 1 Area C: Mixtures of materials applied in Areas A and B in a 50:50 volume ratio in the Test Group

CONTROL GROUP:

Figure 2 Area A: -

Figure 2 Area B: SERUM PHYSIOLOGICAL

Figure 2 Area C: Mixture of SERUM PHYSIOLOGY and FCA (Freund's Complete Adjuvant) at 50:50 volume ratio

Superficial Inducing Phase; On the 7th day after the completion of the intradermal induction phase; To the TEST GROUP; Superficial application is made to the infrascapular region with 8 cm square absorbent gauze to cover the intradermal injection sites. In the Transcutaneous Inducing Phase, the concentration determined in the Test Group Area B is used.

to the CONTROL GROUP; only SERUM PHYSIOLOGICAL is applied.

The dressing and patches are removed after 48 hours.

Stimulation Phase; After the completion of the superficial induction phase, on the 14th day, to the TEST GROUP; Superficial application is made to the untreated areas of the experimental animals and covered with absorbent gauze. In the Intradermal Inducing Phase, the concentration determined in the Test Group Area C is used.

to the CONTROL GROUP; only SERUM PHYSIOLOGICAL is applied. The dressing and patches are removed after 24 hours.

At 24 hours and 48 hours after the completion of the stimulation phase, stimulation sites are observed on the skin of the animals in the test and control groups. Observations are carried out under full spectrum lighting. Skin reactions for Erythema and Edema are completed and graded according to the Magnusson and Kligman grading specified in Table 1 for each time slot for each stimulation site.

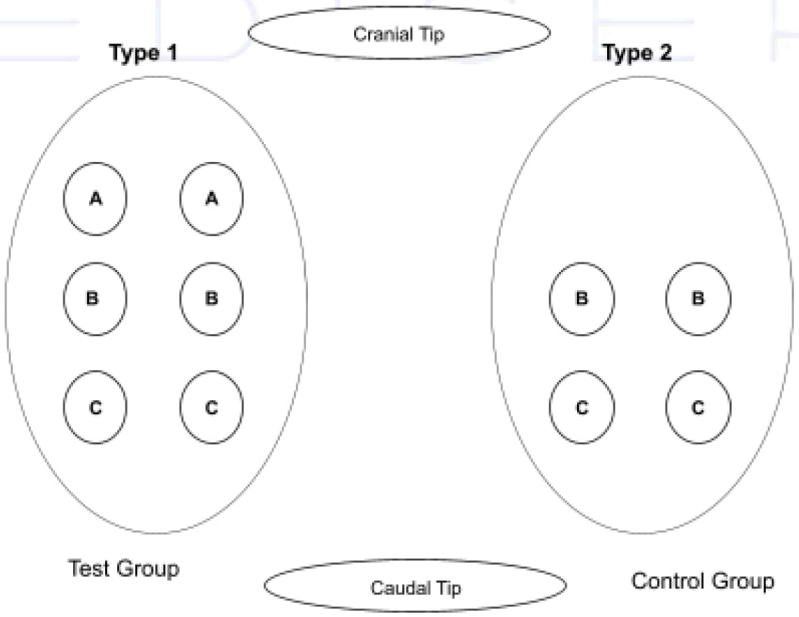

Table 1. Magnusson and Kligman rating scale

Patch Test Reaction	Rating Scale
No visible changes	0
Discrete or patchy erythema	1
Moderate or adjacent erythema	2
Evident	3
Severe erythema or swelling	4

6. EVALUATION

Table 2. Results of the test and control groups at 24 and 48 hours depending on the Magnusson and Kligman rating scale

GROUP	GUINEA PIG NO	AREA	MAGNUSSON AND KLIMMAN RATING ERYTHEMA / PAYMENT	
			EVALUATION TIME POINT	
			24th h	48th h
1cc Felix Filler Dolgu	1	A	2	1
		B	0	0
		C	1	0
	2	A	2	1
		B	0	0
		C	1	1
	3	A	2	1
		B	0	0
		C	1	1
	4	A	2	2
		B	0	0
		C	1	1
	5	A	2	2
		B	0	0
		C	1	1
	6	A	2	1
		B	0	0
		C	1	1
	7	A	2	2
		B	0	0
		C	2	1
	8	A	1	1
		B	0	0
		C	1	0
	9	A	2	1
		B	0	0
		C	1	1
	10	A	2	1
		B	0	0
		C	1	1

GROUP	GUINEA PIG NO	AREA	MAGNUSSON AND KLIMMAN RATING ERYTHEMA / PAYMENT	
			EVALUATION TIME POINT	
			24th h	48th h
CONTROL GROUP	1	A	-	-
		B	0	0
		C	1	1
	2	A	-	-
		B	0	0
		C	1	1
	3	A	-	-
		B	0	0
		C	1	1
	4	A	-	-
		B	0	0
		C	1	1
	5	A	-	-
		B	0	0
		C	1	1

Table 3. Mean Scoring of the values of Table 2

GROUPS	Mean Results
Test Group	0.82
Control Group	0.48

Table 4. End of test weight table of the test animals

TEST GROUP Guinea pig numbers	1	2	3	4	5	6	7	8	9	10
Weights at the end of the test	425	432	437	466	451	431	459	434	499	467
CONTROL GROUP Guinea pig numbers	1		2		3		4		5	
Weights at the end of the test	460		448		435		449		450	

7. RESULT

Following the tests, observations were made in two different time periods as stated. The mean score was obtained by averaging the values obtained. The sensitization score was 0.87 for the sample samples tested. It was determined that the health conditions of the animals were not good and there was no significant weight loss. According to the obtained results, **it was determined that the tested samples do not have sensitizing properties** based on the protocol and evaluation criteria specified in ISO 10993-10.

8. RECORD

All raw data and a copy of the final report are stored in the Medicert archive files.

9. REFERENCES

- Guide for The Care and Use of Laboratory Animals Eighth Edition National Research Council of The National Academies
- TS EN ISO 10993-1 Biological evaluation of Medical Devices - Chapter 1: Evaluation and experiment in a risk management process
- TS EN ISO 10993-2 Biological evaluation of Medical Devices Chapter 2: Conditions for animal welfare
- TS EN ISO 10993-10 Biological evaluation of Medical Devices – Chapter 10: Experiments for irritation and skin sensitivity
- TS EN ISO 10993-12 Biological evaluation of Medical Devices Chapter 12: Sample preparation and reference materials

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