MEDICERT
TESTING LABORATORY
ISO/IEC 17025:2017
IAKS-TL-1018

ISO 10993-10:2014
Skin Irritation Test

IAKS ACCREDITED

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 Irritation 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	**27.02.2022**
Report Number Rapor Numarası	**2023-03/BIYO/1532HA-IRT**
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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INDEX

SUMMARY

Sample **AVAS012023-1** lot number 1 cc Felix Filler Dolgu was tested for biocompatibility according to TS EN ISO 10993-10 Biological evaluation of medical devices - Part 10: Tests for irritation and skin sensitivity. The samples were prepared in SF for 37°C - 72 hours by weighing equal amounts under sterile conditions according to TS EN ISO 10993-12 Biological evaluation of medical devices - Part 12: Sample preparation and reference materials standard. As Positive Control; Sodium lauryl sulfate (SLS), previously known to have an irritant effect, was determined. As Negative Control; Serum Physiologically determined, previously known to have no irritant effect. Three rabbits were used in the study. The observation period was carried out between 06.03.2023 and 09.03.2023. As a result of the analysis, i**t was determined that the test sample did not cause skin irritation**.

1. INTRODUCTION

Purpose : The report described below evaluated the potential of a single topical application for the rabbit skin irritation assay.

Test Guide: This study was carried out according to the requirements of the International Organization for Standardization. 10993: Biological Evaluation of Medical Devices, Part 10: Experiments for Irritation and Skin sensitization.

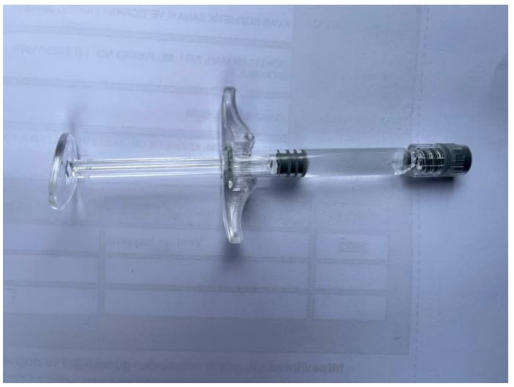
Dates

Sample Acceptance Date : 27.02.2022
Test Date : 06.03.2023
Observation Date : 09.03.2023

2. SAMPLE INFORMATION

Company Name :	Avas Kozmetik
Date of the Sample Acceptance :	27.02.2022 13.05
Sample Record Number :	FLXFHA/202302
Sample Lot Number :	AVAS012023-1
Number of Sample :	4
Packaging Infırmation :	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 :	Rabbit
Strain :	New Zealand
Source :	Burdur Mehmet Akif Ersoy University Experimental Animals Production and Research Center
Gender :	Male
Weight :	2 - 2.5 KG
Age :	4 - 4,5 Months
Acclimation timesi :	5 Days
Number of the animals :	3

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 rabbit 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

Irritation tests were carried out in accordance with ISO 10993-10, care conditions of test animals used in the test, ISO 10993-2, preparation of samples used in the test and reference materials ISO-10993-12.

Test material to be used for irritation tests (specimen) ISO 10993-12 Biological evaluation of medical devices - Part 12: Sample preparation according to the sample preparation and reference materials standard, with 0.2 g / ml sterile 0.9% isotonic in accordance with ISO 10993-12 Prepared at 37 ± 1ºC for 72 ± 2 hours.

As a Positive Control; Sodium Lauryl Sulfate, previously known to have an irritant effect.

As Negative Control; Serum Physiological previously known to have no irritant effect.

Irritation tests were performed on 3 healthy, adult Albino rabbits weighing less than 2 kg. Tests were performed by treating the material to be tested directly on the skin as specified in the ISO 10993-10 standard. After shaving enough to provide sufficient application area (10 cm x 15 cm) in the dorsal region of the experimental animals, the samples were applied as shown in Figure 1.

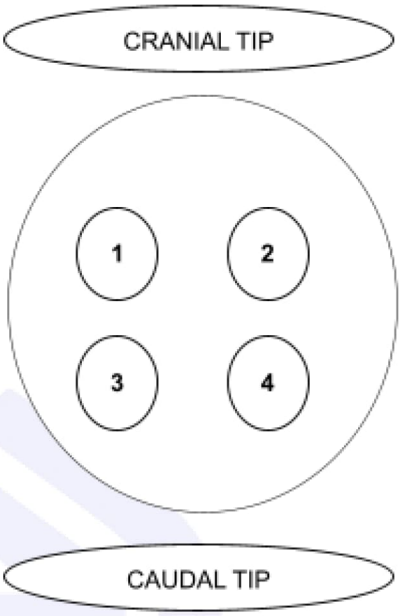


FIGURE 1: Application sides

1. Experimental Side
2. Positive Control
3. Negative Control
4. Experimental Side

6. EVALUATION

Observation results obtained after the test performed in accordance with ISO 10993-10 standards are presented in Table C and Table D. The application areas are indicated with Image 1. With Image 2, redness and edema occurring in the positive control after the application were indicated, and it was stated in the same image whether there was any reaction in the test sample and negative controls. After covering the samples with a 2.5 cm x 2.5 cm sterile gauze cloth, the entire application area was wrapped with a bandage. The samples to be tested for 4 hours were applied to the area.

At the end of this period, the bandages were opened, samples were taken and the applied areas were marked. The test materials remaining in the area were washed with warm water. Experimental areas were observed at 1, 24, 48 and 72 hours after the procedure and samples were evaluated considering the criteria specified in Table A. The evaluation results that should be given according to the scores obtained are presented in Table B.

Table A. Scoring system for skin irritation

Reaction	Score
Erythema and eschar formation	
No erythema	0
Very mild erythema (barely visible)	1
Prominent erythema	3
Moderate erythema	2
Grading erythema with severe erythema (red as beet)	4
Edema formation	
No edema	0
Very mild edema	1
Significant edema (the edges of the area of marked edema)	2
Moderate edema (about 1 mm swollen)	3
Severe edema (swelled more than 1 mm and spread out of the exposed area)	4
Total possible score for irritation	8

Other adverse changes in skin locations should be recorded and reported.

Table B. Irritation categories in rabbits.

Mean Score	Irritation Category
0 - 0.4	Negligible
0.5 - 1.9	Light
2 - 4.9	Middle
5 - 8	Serious

Test Results

Table C. Evaluation Results

Animal No	Samples	Application Side	Observation (h)							
			Erythema				Edema			
			1	24	48	72	1	24	48	72
1	1 cc Felix Filler Dolgu	*Left Front Area*	0	0	0	0	0	0	0	0
		Right Back Area	0	0	0	0	0	0	0	0
	Positive Control	*Right Front Area*	3	2	1	1	1	2	2	1
	Negative Control	*Left Back Area*	0	0	0	0	0	0	0	0
2	1 cc Felix Filler Dolgu	*Left Front Area*	0	0	0	0	0	0	0	0
		Right Back Area	1	0	0	0	0	0	0	0
	Positive Control	*Right Front Area*	3	2	2	2	2	2	1	1
	Negative Control	*Left Back Area*	0	0	0	0	0	0	0	0
3	1 cc Felix Filler Dolgu	*Left Front Area*	1	0	0	0	0	0	0	0
		Right Back Area	0	0	0	0	0	0	0	0
	Positive Control	*Right Front Area*	3	2	2	1	2	2	2	1
	Negative Control	*Left Back Area*	0	0	0	0	0	0	0	0

Table D.Average Score Value

Samples	Primary Irritation Score			Primary Irritation Index
	Rabbit 1	Rabbit 2	Rabbit 3	
1 cc Felix Filler Dolgu	0	0	0	0
Positive Control	1.5	1.67	1.67	1.62
Negative Control	0	0	0	0

7. RESULT

As stated for the test materials, after observations in four different time periods (Table C), the average score was obtained by averaging the obtained values (Table D). No edema or redness was observed in the observations made for the sample specimens tested. In line with the results obtained, **it was determined that the tested sample did not have irritant properties**, based on the protocol and evaluation criteria specified in the ISO 10993-10 document.

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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