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

ISO 10993-11
Pyrogenicity 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	**Pyrogenicity Test**
Test Standard Test Standardı	**TS EN ISO 10993-11 (European Pharmacopoeia, 7th Edition)**
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	**09.06.2023**
Report Number Rapor Numarası	**2023-07/BIYO/1532HA-PT**
Date of Report Rapor Tarihi	**07.07.2023**
Date of Test Deney Tarihi	**21.06.2023 - 23.06.2023**
Report Total Page Raporun Sayfa Sayısı	**8 Sayfa / Page**

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SUMMARY

Sample Felix Filler 1 cc Felix Filler Dolgu with lot number AVAS012023-1 was tested for biocompatibility according to the test standard for ISO 10993-11 (European Pharmacopoeia, 7th Edition) Biological evaluation of medical devices - Pyrogenicity. Since the sample is in gel form, it was applied by mixing with sterile 0.9% saline solution. Three rabbits were used in the study. The observation period was carried out between 21.06.2023 - 23.06.2023. The animals were given pyrogen-free 9 g/L sodium chloride R intravenously for the first three days and their body temperature was recorded. After the samples were mixed with 9 g/L sodium chloride R without pyrogen and given intravenously at a slow rate, body temperatures of the animals were recorded at 30-minute intervals over the next 3 hours. As a result, **it was determined that the test sample did not contain any pyrogen substances.**

1. INTRODUCTION

Purpose: The report described below is aimed at observing the change in body temperature in rabbits administered the sample intravenously.

Test Guide: This study was carried out according to the requirements of the International Organization for Standardization. 10993: Biological Evaluation of Medical Devices, Chapter 11: Systemic Toxicity Tests (European Pharmacopoeia, 7th Edition)

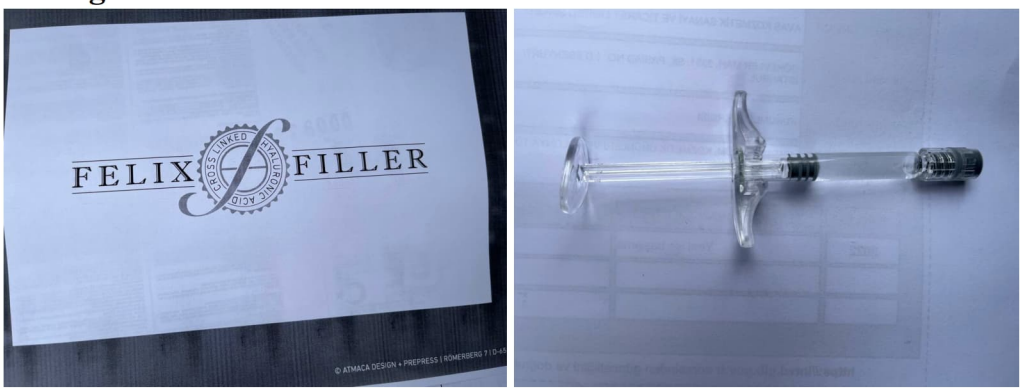
Dates

Sample Acceptance Date : 09.06.2023
Test Date : 21.06.2023
Observation Date : 23.06.2023

2. SAMPLE INFORMATION

Company Name :	Avas Kozmetik
Date of the Sample Acceptance :	09.06.2023 11.02
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 :	One syringe contains 1 cc of Felix Filler filler.
Characteristics of the Sample Use/Application :	

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 :	Female
Weight :	2 - 2.3 KG
Age :	6 Months
Acclimation time :	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 :	Korkutelim brand rabbit feed is given 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

- The pyrogenicity tests (European Pharmacopoeia, 7th Edition), the conditions of care of the experimental animals used in the test, ISO 10993-2 and the preparation of the samples used in the test and the reference materials ISO-10993-12 standards were carried out.
- Pyrogenicity tests were performed on 3 healthy, adult, Albino Rabbits weighing not less than 2 kg.
- Since the test material (sample) to be used for pyrogenicity tests is in gel form, the sample to be administered intravenously was prepared by mixing 0.6 ml sample with 4.4 ml pyrogen-free 9 g/L sodium chloride R solution. All glass sterile disposables were used for injections.
- For rabbits, whose temperature was measured by an electrical device, they were seated in holding boxes and fixed in a normal position. Animals were placed in boxes at least 1 hour before the first recording of temperature and left in them throughout the test.
- Use a thermometer or electrical device that displays the temperature with an accuracy of 0.1°C and is inserted approximately 5 cm deep into the rabbit's rectum.

- After selection of animals, two days before testing the product to be examined, a preliminary test was performed intravenously by heating 10 mL of pyrogen-free 9 g/L sodium chloride R solution per kilogram of body weight to approximately 38.5°C.
- The liquid to be applied for the main test was heated to approximately 38.5°C before injection and 0.6 ml sample was prepared sterile by mixing 4.4 ml of a pyrogen-free 9 g/L sodium chloride R solution. This solution was given intravenously in a slow volume over 2 minutes.
- Using a group of three rabbits for the main test, the temperatures of the animals were recorded at intervals starting at least 90 minutes before injection and continuing for 3 hours after injection of the solution.

6. EVALUATION

The test was performed in a group of three rabbits, whose experimental animal information is listed in Table 1, in accordance with ISO 10993-11 (European Pharmacopoeia, 7th Edition) standards.

Table 1. Test animal information

Animal No	Age	Gender	Weight
1	6 months	Female	2,1 kg
2	6 months	Female	2,3 kg
3	6 months	Female	2,1 kg

The "baseline temperature" of each rabbit was determined as the average of two temperature readings recorded for that rabbit within 40 minutes immediately prior to injection of the product to be examined, and the "maximum temperature" was determined as the highest temperature recorded for that rabbit within 3 hours after injection. All rabbits with an initial temperature greater than 39.8°C or less than 38.0°C should be withdrawn from the test.

Beginning at least 90 minutes before the injection of the product to be examined and continuing for 3 hours after the injection, the body temperature of each rabbit was recorded as indicated in Table 2 at intervals of not more than 30 minutes. The difference between the maximum temperature and the initial temperature of each rabbit was considered the response of the product, and when this difference was negative, the result was counted as a zero response.

Table 2. Test animal body temperature measurements for 100 minutes before injection

Animal No	a	b	c	d	e
1st Rabbit	38.9 °C	39.0 °C	39.2 °C	39.1 °C	39.15 °C
2nd Rabbit	39.1 °C	39.1 °C	39.2 °C	39.2 °C	39.2 °C
3rd Rabbit	39.2 °C	39.2 °C	39.1 °C	39.3 °C	39.2 °C

a. 100 minutes before the injection, b. 80 minutes before the injection, c. 40 minutes before the injection, d. 20 minutes before the injection, e. Initial temperature (average of c and d)

Table 3. Test animal body temperature measurements made for 180 minutes after injection

Animal No	a	b	c	d	e	f	g
1st Rabbit	39.15 °C	39.3 °C	***39.5 °C**	39.4 °C	39.5 °C	39.5 °C	39.4 °C
2nd Rabbit	39.2 °C	39.3 °C	39.3 °C	***39.4 °C**	39.2 °C	39.2 °C	39.3 °C
3rd Rabbit	39.2 °C	39.1 °C	***39.3 °C**	39.2 °C	39.2 °C	39.3 °C	39.3 °C

a. starting temperature, b. 30 minutes after injection, c. 60 minutes after injection, d. 90 minutes after injection, e. 120 minutes after injection, f. 150 minutes after injection, g. 180 minutes after injection

* maximum temperature (highest temperature measured after injection)

6.1. Test Results

If the calculated response of this group based on the results obtained does not exceed the figure given in the second column of Table 4, the item passed the test. If the collected response exceeds the figure given in the third column of the table, the product failed the test. Responses for this product were calculated in Table 5 and the status of the product's response was indicated.

Table 4. Total response and evaluation criteria of the product

Number of rabbits	If the collected response is not exceeded, the product passes	If the collected response is exceeded, the product will fail
3	1.15 °C	2.65 °C
6	2.80 °C	4.30 °C
9	4.45 °C	5.95 °C
12	6.60 °C	6.60 °C

Table 5. Evaluation of total response and product

Animal No.	Initial Temperature (I.T.)	Maximum Temperature (M.T.)	Response (M.T.-I.T.)	Success Status
1	39.15 °C	39.5 °C	0.35 °C	PASS
2	39.2 °C	39.4 °C	0.2 °C	PASS
3	39.2 °C	39.3 °C	0.1 °C	PASS

7. RESULT

In line with the results obtained, the sample was tested according to the method in TS ISO 10993-11 (European Pharmacopoeia, 7th Edition) and **it was determined that the sample did not show pyrogenic properties.**

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 10993-11 (European Pharmacopoeia, 7th Edition)
- TS EN ISO 10993-12 Biological evaluation of Medical Devices - Chapter 12: Sample preparation and reference materials

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Vet. Hek. Simge GARLI	Erol ÜSTÜN	Gonca AÇILMIŞ

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