Hoechst
Pharma Research Toxicology

Report no. 84.0228
May 4, 1984

Perylimid

Testing the acute dermal irritant effects / caustic effects
on rabbits

Dr. N. RUPPRICH
Dr. W. WEIGAND

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1. SUMMARY

Testing the acute dermal irritant effect / caustic effect in rabbits under the described test conditions of the OECD test guidelines has shown that, according to the classification criteria of the EU guidelines, the compound Perylimid is classed as not skin irritating.

2. PRELIMINARY REMARKS

Testing the acute dermally irritating/ caustic effects provides information about the skin irritating or caustic effect of the test compound after single dermal application and serves as the basis for classification and identification.

The present examination has been carried out according to the OECD approved test guideline

OECD Guideline for Testing of Chemicals,
404 Acute Dermal Irritation / Corrosion, OECD 1981

As well as the

OECD principles of best laboratory practices
(Published on February 4, 1983 in the Bundesanzeiger
(German Federal Gazette).

For the purpose of classification of the test compound, the criteria of the

Council Directive dated December 18, 1981 and the Council Directive dating to September 18, 1979 concerning the sixth amendment of the guideline 67/548/EEC concerning the amendment of the legal and administrative regulations for the classification, packaging and identification of hazardous compounds. Annex VI, Council Directive 79/831/EEC.

During the text, there were no unforeseen circumstances that may have affected the quality and integrity of the present test.

3. OVERSIGHT

Test No.:	84.0215
Test compound:	Perylimid
Customer:	Farben Nord, Werk Höchst
Animal species:	New Zealand albino rabbits
Test start:	April 10, 1984
Test end:	April 13, 1984
Dose:	500 mg

R E S P O N S I B L E:

Industrial toxicology:	Dr. WEIGAND
Test director:	Dr. RUPPRICH
Unit GLP:	Ap. HARSTON
Testing and archiving unit:	Pharma Research Toxicology PO Box 80 03 20 6230 Frankfurt 80

4. MATERIAL AND METHODOLOGY

4.1 Test compound

Commercial name:	Perylimid
Code:	EMGW 9956
Application type:	Pigment intermediate
Chemical name:	Perylen-3, 4, 9, 10-tetracarbonaciddiimide
Molecular formula:	C_{24} H_{10} N_2 O4
Mol mass:	390
Appearance:	Blackish-brown powder
Melting point:	400 °C
pH value in water:	9 (due to the K0H content)
Solubility:	Water solubility: Only the contaminations are soluble Liposolubility: not soluble In other solvents: not soluble
Composition:	Approx. 80% Perylimid Approx. 10% K0H Approx. 8% diverse organic contaminations Approx. 1% inorganic salts Approx. 1% water
Batch number and production Date:	Op.69/March83
Storage :	In a dark place at approx. 22 °C

4.2 Animal species and husbandry conditions

Animal species:	New Zealand albino rabbits
Strain:	Hoe: HIMK (SPFWiga)
Origin:	HOECHST AG, Kastengrund, conventional breeding
Number of animals:	3
Identification of the animals:	Numbered ear marks
Animal weight:	2.7 – 3.5 kg
Animal husbandry:	In fully climatized rooms in individual cages (battery husbandry)
Room temperature:	20 ± 2 °C
Relative humidity:	55 ± 10%
Lighting duration:	12 hours daily
Food:	Altoromin 2123 Haltungsdiät - rabbit food Altoromin GmbH, Lage/Lippe, ad libitum
Water:	Deionised water with chlorine from automatic drippers, ad libitum

4.3 Test groups

Approximately 24 hours prior to the start of the experiment, approximately 25 cm^2 of fur of 3 rabbits was removed in the dorsal and lateral areas of the torso using an electric shaving device. Only animals with unblemished skin were used.

At the start of the test, 500 mg of Perylimid, added to 0.3 ml of 0.9% NaCl solution, were applied to 2.5 x 2.5 cm plaster cellulose pads (especially manufactured by the company Baiersdorf AG, Hamburg). The plasters were fixed onto the previously shaved spots and covered with a semi-occlusive bandage.

The exposure time was 4 hours. After the exposure period, the remaining test compound was carefully removed from the skin.

The first evaluation occurred within 30 – 60 minutes after removing the plaster, further evaluations occurred after 24, 48 and 72 hours after removing the plaster.

The formation of erythema and edema was numerically evaluated according to the Draize-method. All further toxicologically important findings were recorded.

4.4 Evaluation

Median values for the erythema and edema of all animals were established from the individual values for the formation of erythema and edema formation at the observation intervals of 24 hours, 48 hours and 72 hours. If both median values were lower than 2, the median values for the formation of erythema and edema were calculated for each animal.

The following criteria apply for classifying the test compound as “caustic” or “skin irritant”:

A test compounds is caustic if the healthy intact skin of at least one test animal is destroyed in its entire thickness when applying the test compound.

A test compound is skin irritant if it causes an inflammation of the skin which occurs after maximum 4 hours of exposure time and lasts at least 24 hours and corresponds to the following values:

1. The median value for the formation of erythema and scabs or of edema across all test animals is at least 2 or higher
2. When carrying out the test with 3 test animals, at least 2 test animals have a median value for the formation of erythema and scabs or an edema of at least 2 or higher.

5. RESULTS

The exposure time for the added compound on the rabbit skin was 4 hours.

30 minutes to 48 hours after removing the skin patches, very slight, barely visible erythema were found. Two animals showed small, reddish-brown skin discoloration. 72 hours after the exposure, no animal shows any signs of a skin irritation.

The following median values were calculated from the numerically evaluated individual findings concerning the formation of erythema and edema at the observation points after 24 hours, 48 hours and 72 hours:

Formation of erythema and scabs	All animals:	0.4
	Animal 1:	0.7
	Animal 2:	0.7
	Animal 3:	0
Edema formation	All animals:	0
	Animal 1:	0
	Animal 2:	0
	Animal 3:	0

According to the classification criteria of the EU guideline and taking into account all toxicologically relevant findings, the compound Perylimid is considered as non-skin irritant.

Dr. Ru/Ri

Unit GLP

Pharma Research Toxicology
of the
HOECHST AKTIENGESELLSCHAFT

Dr. Rupprich
Test director

Dr. Weigand
Coordination industrial toxicology

6. Table 1: Acute dermal irritant effect / caustic effect

Individual findings after single dermal application of Perylimid

Time after Patch removal:	0.5 h – 1 h	24 h	48h	72h
Animal no.:	1 2 3	1 2 3	1 2 3	1 2 3
Erythema:	1 1 1	1 1 0	1 1 0	0 0 0
Edema:	0 0 0	0 0 0	0 0 0	0 0 0
Skin discoloration Small area Reddish-brown	x x	x x	x x	

7. Evaluation key

Evaluation of skin reactions according to Draize

Formation of erythema and scabs

No erythema	0
Very slight, barely visibly erythema	1
Pronounces erythema	2
Moderate to serious erythema	3
Serious erythema (dark read) to light scab formation (injury in the deeper skin layers)	4

Formation of edema

No edema	0
Very slight, barely visible edema	1
Slight edema. Edges are clearly visible	2
Moderate edema, raised by approx. 1 mm	3
Serious edema, raised by more than 1 mm and exceeding the limits of the application site	4

Hoechst Corporation
Pharma research
Unit GLP

May 11, 1984

Title: Perylimid
Testing the acute dermal irritant effects / caustic effects on rabbits

Date: May 4, 1984

Test no: 84.0215

This test has been inspected regularly and the written, duly signed documentation has been presented to the directors of the test institutions and the test directors as follows:

Inspection	Report
April 10, 1984	April 10, 1984
April 10, 1984	April 10, 1984
May 11, 1984	May 11, 1984

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Unit GLP

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