Hoechst
Pharma Research Toxicology

Report no. 84.0225
May 2, 1984

Corresponds to study #11 in Attachment A of transmittal memo on CBI
HERO ID:4731531

Perylimid

Testing the acute oral toxicity
in the male and female wistar rat

Dr. N. RUPPRICH
Dr. W. WEIGAND

CONTENTS

1. SUMMARY

In testing the acute oral toxicity of Perylimid in the Wistar rat, for male and female animals the medium lethal dose (LD50) was above 5000 mg/kg bodyweight. When giving 5000 mg/kg bodyweight, neither male nor female animals showed any signs of intoxication. There was no lethality.

Based on the acute oral toxicity test on the male and female Wistar rat, the given compound Perylimid is not subject to labelling.

2. PRELIMINARY REMARKS

Determining the acute oral toxicity represents the first step in characterising the toxicological characteristics of a compound. It provides information about the health risks for a single oral ingestion and serves as a basis for classification. It enables a reasonable choice of dose when examining the toxicity with repeated application of the testing compound. The Wistar rat has proven itself as a suitable species for testing the acute oral toxicity of a range of different compounds.

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

OECD Guideline for Testing of Chemicals, 401
"Acute Oral Toxicity", OECD 1981

As well as the test guideline currently discussed by the EC

EEC Directive 79-831, Annex V, Part B :
Methods for the Determination of Toxicity
4.1.1 Acute Toxicity Orally

And according to the

OECD Principles of Best Laboratory Practice
(Announcement dating to February 4, 1983
In the Bundesanzeiger (German Federal Gazette)

The classification of the test compound occurs according to the regulation concerning the indications of danger of substances and compounds according to the Chemical Act (ChemG Gefährlichkeitsmerkmale-V) 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 type:	Acute oral toxicity
Animal species/gender:	Wistar rat, male and female
Test no:	84.0214
Test compound:	Perylimid
Customer:	Farben Nord, Werk Höchst
Test start:	April 11, 1984
Test end:	April 25, 1984

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 HOECHST CORPORATION 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:	Wistar rat
Strain:	Hoe WISKf (SPF71)
Origin:	HOECHST AG, Kastengrund, SPF breeding
Body weight at test start:	
Male animals:	X = 166.6 g (= 100%) X min = 161 g (-3.4%) X max = 173 g (3.8%)
Female animals:	x = 182.2 g (= 100%) X min = 178 g (-2.3%) X max = 190 g (+4.3%)
Randomization:	According to schedules 131/84 and 132/84
Animal husbandry:	In fully climatized rooms in macrolon cages (type 4) on soft wood granules in groups of up to 5 animals
Room temperature:	22 ± 2 °C
Relative humidity:	55 ± 10%
Lighting duration:	12 hours daily
Acclimatization:	At least 5 days
Food withholding:	16 hours prior and 2 hours following application
Food:	Rat food Altromin 1324 (Altromin-GmbH, Lage/Lippe), ad libitum
Water:	Tap water in plastic drinking bottles at libitum
Identification of animals:	Fur marking with $KMn0_4$ and numbering the cages

4.3 Test groups

The acute oral toxicity of Perylimid in the wistar rat was only tested for the dose of 5000 mg/kg body weight. Should no compound-related lethality occur in this short test, a detailed test of the acute oral toxicity of the test compound will not be necessary according to current guidelines.

Dose in mg/kg body weight	Concentration in % (w/v)	Application volume in ml/kg body weight	Number of animals male	female
Carrier: 2% starch-sludge				
5000	25	20	5	5

4.4 Carrying out the test

The test compound was suspended in the starch sludge and given to the animals by means of a gavage. For dosing plan see item 4.3. After the treatment, the course of the toxication, the lethality rate and the dying off time were determined. In the subsequent 14-day observation period, the animals were weighed weekly. At the end of the observation period, the animals were killed with CO_2 gas, dissected and in addition, examined for macroscopically visible changes.

5 RESULTS

5.1 Lethality and LD50

Dose in mg/kg body weight	Concentration in % (w/v)	Application volume in ml/kg bodyweight	Lethality in male animals	Lethality in female animals
5000	25	20	0/5	0/5

During the 14-day post-observation period, neither male nor female animals died. As a result of the present test of the acute oral toxicity of Perylimid in the wistar rat, for male and female animals the medium lethal dose (LD50) was above 5000 mg/kg bodyweight.

5.2 Clinical toxic reactions

Neither male nor female animals showed any symptoms of being poisoned.

There was no reduction in the development of body weight (see Annex 6.1).

5.3 Dissection findings

The animals killed at the end of the post-observation period showed not macroscopically visible changes (see Annex 6.1).

Dr. Ru/Ri

Unit GLP

Pharma Research Toxicology of the
HOECHST AKTIENGESELLSCHAFT

Dr. Rupprich
Test director

Dr. Weigand
Coordination industrial toxicology

6 ANNEX

6.1 Individual results

Test no: 84.0214
Compound: Perylimid
Dose: 5000 mg/kg body weight
Application form: 25% in starch sludge
Application type: per os
Species/Gender: Wistar rat / male

Development of body weight

Animal no.	at test start	after 7 days		after 14 days	
	g	g	%	g	%
1	165	225	+36.4	259	+57.0
2	164	216	+31.7	246	+50.0
3	173	225	+30.6	252	+45.7
4	161	211	+31.1	254	+57.8
5	170	217	+27.6	238	+40.0

Clinical toxicity reactions

Time after from:	0’	10’	30’	1h	2h	4h	1d	2d	3d	4d
application to:	10’	30’	60’	2h	4h	6h	1d	2d	3d	14d
Lethality rate	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5
	Number of animals with symptoms									
No clinical poisoning symptoms	5	5	5	5	5	5	5	5	5	5

Dissection findings

5 animals killed at test end: without any macroscopically visible features

6 ANNEX

6.1 Individual results

Test no:	84.0214
Compound:	Perylimid
Dose:	5000 mg/kg body weight
Application form:	25% in starch sludge
Application type:	Per os
Species/Gender:	Wistar rat / female

Development of body weight

Animal no.	at test start	after 7 days		after 14 days	
	g	g	%	g	%
1	178	198	+11.2	204	+14.6
2	190	209	+10.0	217	+14.2
3	182	212	+16.5	223	+22.5
4	180	204	+13.3	214	+18.9
5	181	200	+10.5	198	+ 9.4

Clinical toxicity reactions

Time after from:	0’	10’	30’	1h	2h	4h	1d	2d	3d	4d
Application to:	10’	30’	60’	2h	4h	6h	1d	2d	3d	14d
Lethality rate	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5
	Number of animals with symptoms									
No clinical poisoning symptoms	5	5	5	5	5	5	5	5	5	5

Dissection findings

5 animals killed at test end: without any macroscopically visible features

Hoechst Corporation
Pharma research
Unit GLP

May 22, 1984

Title: Perylimid
Testing the acute oral toxicity in the male and female wistar rat

Date: May 2, 1984

Test no: 84.0214

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 11, 1984	April 11, 1984
May 22, 1984	May 22, 1984

Pharma Research
Unit GLP