REACH

Tetrasodium 1-acetamido-2-hydroxy-3-(4-((4-sulphonatophenylazo)-7-sulphonato-1-naphthylazo))naphthalene-4,6-disulphonate

EC number: 219-746-5 | CAS number: 2519-30-4

Toxicological information

Repeated dose toxicity: oral

001 Weight of evidence | Experimental result

Administrative data

Endpoint:	repeated dose toxicity: oral
Remarks:	combined repeated dose and carcinogenicity
Type of information:	experimental study
Adequacy of study:	weight of evidence
Reliability:	2 (reliable with restrictions)

Data source

Reference

Reference Type:	publication
Title:	LONG-TERM TOXICITY STUDY OF BLACK PN IN MICE
Author:	J.-P. DRAKE, K. R. BUTrERWORTH, I. F. GAUNT and P. GRASSO
Year:	1977
Bibliographic source:	Food and cosmetics toxicology; Vol 15, pp. 503-508, Pergamon Press 1977

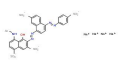
Materials and methods

Principles of method if other than guideline:	A repeated dose study investigating the effect of Brilliant Black PN in CFW strain mice when administered orally for 80 wk.
GLP compliance:	not specified
Limit test:	no

Test material

Test material information

Constituent 1



Reference substance name:	Tetrasodium 1-acetamido-2-hydroxy-3-(4-((4-sulphonatophenylazo)-7-sulphonato-1-naphthylazo))naphthalene-4,6-disulphonate
EC Number:	219-746-5
EC Name:	Tetrasodium 1-acetamido-2-hydroxy-3-(4-((4-sulphonatophenylazo)-7-sulphonato-1-naphthylazo))naphthalene-4,6-disulphonate
Cas Number:	2519-30-4
Molecular formula:	C28H21N5O14S4.4Na
IUPAC Name:	tetrasodium 4-acetamido-5-hydroxy-6-({7-sulfonato-4-[(4-sulfonatophenyl)diazenyl]-1-naphthyl}diazenyl)naphthalene-1,7-disulfonate

Test material form:	solid: particulate/powder
Remarks:	migrated information: powder
Details on test material:	- Name of test material (as cited in study report): Brilliant Black PN- Molecular formula (if other than submission

substance): C28H17N5Na4O14S4- Molecular weight (if other than submission substance):867.66716 g\mol - Substance type: Organic- Physical state: Solid

Test animals

Species:	mouse
Strain:	other: CFW strain
Sex:	male/female
Details on test animals or test system and environmental conditions:	TEST ANIMALS- Source: From a specified-pathogen-free colony- Age at study initiation: No data available- Weight at study initiation: The mice were weighed at the start of the experiment (exact weight not mentioned)- Fasting period before study: No - Housing: They were caged in groups of 15 in a room- Diet (e.g. ad libitum): Oxoid pasteurized breeding diet,ad libitum- Water (e.g. ad libitum): ad libitum- Acclimation period: No data availableENVIRONMENTAL CONDITIONS- Temperature (°C): 21±1°C- Humidity (%):50-60%- Air changes (per hr): No data available- Photoperiod (hrs dark / hrs light): No data available

Administration / exposure

Route of administration:	oral: feed
Vehicle:	not specified
Details on oral exposure:	No data
Analytical verification of doses or concentrations:	not specified
Duration of treatment / exposure:	80 wk
Frequency of treatment:	Daily

Doses / concentrations

Remarks:	Doses / Concentrations:0.1, 0.25,0.5 or 1.0% (130,325,650,1300 mg/kg bw/d)Basis:no data

No. of animals per sex per dose:	30 male and 30 female mice
Control animals:	yes
Details on study design:	No data available
Positive control:	No data available

Examinations

Observations and examinations performed and frequency:	CAGE SIDE OBSERVATIONS: Yes - Time schedule: in groups of 15 in a roommaintained at 21 ± 1°C with a relative humidity of 50-60%- Cage side observations checked in table [No.?] were included.: No dataDETAILED CLINICAL OBSERVATIONS: No data- Time schedule: No dataBODY WEIGHT: Yes - Time schedule for examinations: start of the experiment, at wk 3 and then at intervals of 2 wk until wk 73 of the experimentFOOD CONSUMPTION AND COMPOUND INTAKE (if feeding study):- Food consumption for each animal determined and mean daily diet consumption calculated as g food/kg body weight/day: No data- Compound intake calculated as time-weighted averages from the consumption and body weight gain data: No dataFOOD EFFICIENCY:- Body weight gain in kg/food consumption in kg per unit time X 100 calculated as time-weighted averages from the consumption and body weight gain data: No dataWATER CONSUMPTION AND COMPOUND INTAKE (if drinking water study): No data- Time schedule for examinations: No dataOPHTHALMOSCOPIC EXAMINATION: No data - Time schedule for examinations: No data- Dose groups that were examined: No dataHAEMATOLOGY: Yes - Time schedule for collection of blood:At wk 28 and 55 from the caudal vein of ten males and ten females from the control group and from the groups of 0.5 and 1.0% dietary levels.At 80 wk, blood samples were collected from the aorta of all surviving mice during the autopsy.- Anaesthetic used for blood collection: No data- Animals fasted: No data- How many animals: 20 animals (10 male and 10 female)- Parameters were examined: counting the reticulocyte and leucocytes.CLINICAL CHEMISTRY: No data- Time schedule for collection of blood: No data- Animals fasted: No data- How many animals: No data- Parameters were examined: No dataURINALYSIS: Yes - Time schedule for collection of urine: At 28 wks at 6-hr period from three groups of five mice of each sex from the controls and the groups on the two highest dietary levels (0.5 and 1.0%) of Black PN.- Metabolism cages used for collection of urine: No data-

	Animals fasted: No data- Parameters were examined: reducing substances, bile salts and blood as well as for colour, pH and microscopic constituentsNEUROBEHAVIOURAL EXAMINATION: No data - Time schedule for examinations: No data- Dose groups that were examined: No data- Battery of functions tested: sensory activity / grip strength / motor activity / other: No data
Sacrifice and pathology:	GROSS PATHOLOGY: no dataHISTOPATHOLOGY: Yes
Other examinations:	Carcinogenic examination
Statistics:	chi-square test, Student's t test

Results and discussion

Results of examinations

Clinical signs:	no effects observed
Mortality:	no mortality observed
Body weight and weight changes:	no effects observed
Food consumption and compound intake (if feeding study):	not specified
Food efficiency:	not specified
Water consumption and compound intake (if drinking water study):	not specified
Ophthalmological findings:	not specified
Haematological findings:	not specified
Clinical biochemistry findings:	not specified
Urinalysis findings:	no effects observed
Behaviour (functional findings):	not specified
Organ weight findings including organ / body weight ratios:	no effects observed
Gross pathological findings:	not specified
Histopathological findings: non-neoplastic:	no effects observed
Histopathological findings: neoplastic:	not specified
Details on results:	CLINICAL SIGNS AND MORTALITY:No effect on the condition or behaviour of the animals.There were no statistically significant differences between the number of deaths in the control mice and those given Black PN.BODY WEIGHT AND WEIGHT GAIN:The body weights of mice of both sexes were similar in all groups and No dose related effects on weight gain.FOOD CONSUMPTION AND COMPOUND INTAKE (if feeding study):No data availableFOOD EFFICIENCY:No data availableWATER CONSUMPTION AND COMPOUND INTAKE (if drinking water study):No data availableOPHTHALMOSCOPIC EXAMINATION:No data availableHAEMATOLOGY:No data availableCLINICAL CHEMISTRY:No data availableURINALYSIS:No abnormal constituents were detected in the urine from the control or treated mice.NEUROBEHAVIOUR:No data availableORGAN WEIGHTS:Scattered differences in mean organ weights between treated and control animals.A lower brain weight in females, compared with the control value, was the only difference affecting animals fed 1% Black PN.The relative brain weight of females fed 0.25% Black PN was higher than the control figure. Liver weights of female but not of male mice fed 0.25% Black PN were lower than control values, but again this was an isolated finding and there were no significant differences in relative liver weights. Kidney weights of male animals only were significantly lower than control values at the two lowest levels of treatment (0.1 and 0.25%), but a significant difference in relative kidney weights of males occurred only at the 0.5% level, at which a higher value was recorded for the treated mice. The only other significant differences occurred in the relative heart weights, which were raised in male mice fed 0.5% and in females fed 0.25% Black PN.The changes in organ weight showed no dose related effects. Moreover the isolated changes seen at the lower levels were not found in both sexes and were not evident when expressed relative to body weight. It is considered that these random findings were not associated with Black PN treatment.GROSS PATHOLOGY:No data availableHISTOPATHOLOGY: NON-NEOPLASTIC:Most of the tumours in the study occurred with either a comparable or a greater incidence in the control groups than in the treated mice .Several isolated tumours were identified in mice given the

lower levels of Black PN, without comparable findings in the controls or in the highest dose group. Mammary fibroadenoma, a uterine fibromyoma, squamous-cell carcinoma were seen at different concentration.The frequency of histopathological findings in the treated animals did not differ significantly from those in the controls. Hence, no relationship was obvious between these findings and treatment with Black PN. Only in the case of adenomas of the lung and of the mammary tissue did more than one tumour of a given type occur among the treated animals of any group.

Effect levels

Dose descriptor:	NOAEL
Effect level:	1 300 other: mg/kg/day
Based on:	test mat.
Sex:	male/female
Basis for effect level:	other: Body weight, weight gain, organ weight and histopathology.

Target system / organ toxicity

Critical effects observed:	not specified

Applicant's summary and conclusion

Conclusions:	The endpoint for the repeated dose toxicity by oral route was found to be NOAEL at 1 % (1300 mg/kg/day) concentration of Black PN to mice.
Executive summary:	Repeated dose toxicity test were performed on mice with different concentrations from 0.1, 0.25,0.5 or 1.0% (130,325,650,1300 mg/kg bw/d)Black PN for 80 wk. 30 males and 30 females was used for the treatment and group of 60 mice of each sex as control. The general condition and behaviour of the animals were observed frequently and any mouse that showed signs of ill-health was isolated, to be returned to its cage on recovery or to be killed if its condition deteriorated. The mice were weighed at the start of the experiment, at wk 3 and then at intervals of 2 wk until wk 73 of the experiment. Blood sample were taken at wk 28 and 55.At 80 wk, blood samples were collected from the aorta of all surviving mice during the autopsy. For haematology blood samples were collected and for urine sample from 6-hr period from three groups of five mice of each sex from the controls and the groups on the two highest dietary levels of Black PN. Histopathology was also conducted. There were no dose-related effects on body-weight gain, haematology or organ weights. The incidence of histopathological findings, including tumours, was not altered by the feeding of Black PN. Therefore, the endpoint for the repeated dose toxicity was found to be NOAEL at 1 % (1300 mg/kg/day) concentration of Black PN to mice.