

8EHQ-1004-15754



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October 13, 2004

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To Whom It May Concern:

PPG Industries Inc., (PPG) is submitting this information pursuant to Section 8(e) of TSCA.

PPG is submitting draft summary information concerning two toxicology studies with respect to WRS-2390, CAS# 68227-46-3, an isolated intermediate chemically converted in subsequent production of a resin that is a component of an electrodeposition coating.

The final report will be provided to the EPA once received by PPG.

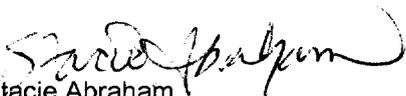
As a part of EPA's high production volume challenge program, toxicity studies were conducted on WRS-2390. In a 4-week toxicity study, four groups of 5 male and 5 female rats were dosed daily for 4 weeks by oral gavage at levels of 0, 2, 7.5, and 30 mg/kg/day. Reduction in body weight gain and food consumption was noted throughout the study period at 7.5 mg/kg/day. Decreased body weight gain and food consumption was only noted during the first week of the study in both sexes dosed at 30 mg/kg/day. Upon a microscopic evaluation, treatment related effects on testes and epididymides (*see attached for details*) were observed in 2 males treated with 30 mg/kg/day.

In a subsequent reproduction/developmental toxicity screening study, four groups of 10 male rats were treated by oral gavage at levels of 0, 2, 7.5, and 50 mg/kg/day for 2 weeks prior to mating, through until necropsy after at least 4 weeks of treatment. Females were treated similarly for 2 weeks prior to mating, then through mating, gestation and until day 4 of lactation. At 50 mg/kg/day level, decreased body weight gain and food consumption was observed during the first week of the study. There were decreases in testes and epididymides weights. Upon a microscopic evaluation, treatment related effects on testes and epididymides (*see attached for details*) were observed in 6 males. All pups from this group died shortly after birth. No treatment related effects on testes and epididymides were noted in animals treated with 2 or 7.5 mg/kg/day.

PPG provides our associates with labels and MSDS, which specify procedures for proper handling and disposal of this material including the use of personal protective equipment.

Please telephone me at [412 492-5308] if you have any questions.

Sincerely yours,


Stacie Abraham
Senior Product Safety Analyst
North America and European Regions
PPG Industries, Inc.



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Stacie Abraham

attachments

280078

1 Summary

The test item, WRS-2390TX, was accepted from PPG Industries, Incorporated. The objective of this study was to assess the toxicity of the test item in the rat after oral administration by gavage for 4 weeks.

Three groups of 5 male and 5 female (Low, Intermediate and High dose groups) Sprague-Dawley rats were dosed daily for 4 consecutive weeks by gavage at levels of 2, 7.5 and 30 mg.kg⁻¹.day⁻¹. A further group of 5 male and 5 female Sprague-Dawley rats received vehicle (water for irrigation) only and acted as a Control group.

The animals were monitored daily for any signs of ill health or reaction to treatment. Detailed functional observations were performed once during pretrial and during Week 4 of treatment. Additional detailed functional observations were also conducted during pretrial and once weekly up until Week 4. Body weights were recorded once during Pretrial then daily throughout dosing (twice weekly data reported). Food consumption was recorded twice weekly during pretrial and throughout treatment. Water consumption was assessed visually on a weekly basis. Ophthalmoscopic assessments were undertaken on all animals during pretrial and on all Control and High dose animals during Week 4. Urine and blood samples were both collected for laboratory investigations during Week 4.

After 4 weeks of treatment, all animals were killed and necropsied. All animals were given a detailed post mortem examination with major organs being weighed and/or placed in fixative. Tissues from all Control and High dose animals and testes and epididymides from all male animals were examined histologically.

There was 1 premature decedent during the study. Retrobulbar haemorrhage secondary to orbital venipuncture was considered to be the cause of death and was not considered to be related to treatment with WRS-2390TX.

Daily oral dosing with WRS-2390TX for 4 consecutive weeks resulted in an overall reduction in body weight gain and food consumption performance in both sexes treated at 7.5 mg/kg/day. Decreased body weight gain and food consumption were also observed up to Day 7 of treatment in both sexes dosed at 30 mg/kg/day. However from Day 10 of treatment onwards, group mean body weight and food consumption in animals treated at 30 mg/kg/day were comparable with Controls. Due to the lack of a dose related effect, the implications of reduced body weight and food consumption performance in animals treated at 7.5 mg/kg/day are unclear.

Isolated incidences of excess salivation were noted throughout the study in a number of animals treated at 30 mg/kg/day. There were no other in-life findings that were considered to be related to treatment with WRS-2390TX.

Tubular atrophy was found in the testes of 3 animals given 30 mg/kg/day. In Animal 20 this was accompanied by unilateral agenesis of the epididymis. As a spontaneously occurring finding, unilateral agenesis of the epididymis would be expected to result in tubular atrophy of the testis on the same side. In the 2 other High dose group animals

with bilateral tubular atrophy in the testes, sloughing of spermatogenic cells was found in the epididymides.

There were no findings in testes and epididymides of animals treated at 7.5 mg/kg/day.

Spermatid retention and marked tubular atrophy were found in the testes of Animals 8 and 9 respectively. These animals also had oligospermia or sloughing of spermatogenic cells in the epididymides. Available organ weight data confirm histology data.

However, there were no histological findings seen in the testes and epididymides of animals treated at 2 or 7.5 mg/kg/day in a subsequent Reproduction/Developmental Toxicity Screening Test in Rats (Inveresk study 493506) which dosed a similar strain/age of animals as used in this study.

In conclusion, there was some evidence of an effect on testes and epididymides of animals given 30 mg/kg/day. Due to the lack of a clear dose relationship, it could not be concluded that the findings in testes and epididymides in animals given 2 mg/kg/day were related to administration of WRS-2390TX.

WRS-2390TX

Reproduction/Developmental Toxicity Screening Test in Rats

Inveresk Project No: 493506

PATHOLOGY REPORT

Draft

Total Number of Pages 4

Summary

Necropsy Findings

Small, flaccid testes and small epididymides were seen in some males given 50 mg/kg/day.

Histology Findings

There was severe seminiferous epithelial degeneration associated with mild interstitial cell hyperplasia in the testes of some males given 50 mg/kg/day, together with oligospermia and sloughing of spermatogenic cells in the epididymides.

Introduction

The data described in this report was generated by direct computer entry using Places Software supplied by Instem.

The data output on which this report is based and which are to be included in the Study Report are listed below.

PLAFOR_493506_MACRO_LL_KEEP1
PLAFOR_493506_MICRO_PR_TEMP2

Experimental Procedure

Definitions

Only standard pathological terminology was used.

Statistical Methods

The statistical values referred to here and marked on the incidence table are the result of Fisher's Exact test (two-tailed).

Peer Review

All tissues from animals 31-34 and 77-80 and testis and epididymis from animals 21-30 were examined by a second pathologist. The data in this report reflect the consensus view of the Study Pathologist and Reviewing Pathologist.

Results

Necropsy Findings

The testes were small in 6/10 males given 50 mg/kg/day, and also flaccid in 3 of these animals. In one animal, the epididymides were small as well.

Histology Findings

There was severe seminiferous epithelial degeneration in 6/10 males given 50 mg/kg/day, which correlated with the small, flaccid testes seen at necropsy. These animals also showed mild testicular interstitial cell hyperplasia. There was oligospermia and sloughing of spermatogenic cells in the epididymides from the same animals, which in one animal correlated with small epididymides at necropsy. Minimal sloughing of spermatogenic cells was also present in the epididymides of one male given 7.5 mg/kg/day.

Discussion

Findings in the testes and epididymides in males given 50 mg/kg/day correlated with reductions in weight which were statistically significant when compared with Group 1.

Minimal sloughing of spermatogenic cells in the epididymides of one male given 7.5 mg/kg/day was not considered to provide sufficient evidence of an effect of treatment, as this finding could have occurred spontaneously.

Conclusion

Administration of WRS-2390TX at 50 mg/kg/day was associated with severe seminiferous epithelial degeneration in the testes, together with oligospermia and sloughing of spermatogenic cells in the epididymides.

The no effect level was 7.5 mg/kg/day.

Signed: _____

Date: _____

Petrina Rogerson BVMS, MRCVS

Document History

Version Draft

References

21-5133

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