

CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA

BIOBOR JF¹

2,2-oxybis (4,4,6-trimethyl-1,3,2-dioxaborinane) [CC 792] combined with
2,2-(1-methyltrimethylenedioxy)bis-(4-methyl-1,3,2-dioxaborinane) [CC 2227]

2,2-oxybis(4,4,6-trimethyl-1,3,2-dioxaborinane)
Chemical Code # 000792, Tolerance # 50439

July 25, 2003

I. DATA GAP STATUS

Chronic Toxicity, rat:	Data gap, no study on file
Subchronic, dermal, rabbit	Data gap, upgradeable study, dermal irritation
Chronic Toxicity, dog:	Data gap, no study on file
Oncogenicity, mouse:	Data gap, no study on file
Oncogenicity, rat:	Data gap, no study on file
Reproduction, rat:	Data gap, no study on file
Reproduction, mouse:	Data gap, no study on file
Teratology, rat:	No data gap, possible adverse effect
Teratology, rabbit:	Data gap, inadequate study, possible adverse effect indicated
Gene mutation:	No data gap, no adverse effect
Chromosome:	Data gap, inadequate study on file, no adverse effect indicated
DNA damage:	Data gap, inadequate study, no adverse effect indicated
Neurotoxicity:	Not required at this time

Toxicology one-liners are attached.

** indicates an acceptable study.

Bold face indicates a possible adverse effect.

Toxicology summary by Kishiyama and Gee, 7/25/03.

File name: T030725.

See also the "Reregistration Eligibility Document" of US EPA, dated June, 1993. There is currently one product registered in California, Biobor JF.

¹ See file Grouping.doc

II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

These pages contain summaries only. Individual worksheets may contain additional effects.

COMBINED, RAT

No study on file.

CHRONIC TOXICITY, RAT

No study on file.

CHRONIC TOXICITY, DOG

No study on file.

ONCOGENICITY, RAT

No study on file.

ONCOGENICITY, MOUSE

No study on file.

REPRODUCTION, RAT

No study on file.

TERATOLOGY, RAT

** **002 088735** Lemen, J. K. "Rat teratology Study with Biobor® JF." (Hazleton Laboratories America Incorporated, HLA Study No. 182-129, July 12, 1990.) BIOBOR® JF, purity 95%, was administered by gavage at doses of 0 (corn oil), 100, 300, or 1000 mg/kg to 25 mated female Crl:CD®BR rats per group 6 through 15 of gestation. Test article was not corrected for purity. **Possible adverse effect:** lower fetal weights and viability; increased incidence of soft tissue variations (dilated ventricles of the brain and renal pelvic cavitation); fetal skeletal variations (incomplete ossified and/or unossified skull, vertebrae, sternbrae, centra, ischium, pubes, metacarpals, metatarsals); vertebral anomalies with and/or without associated rib anomalies - malformations. Developmental NOEL = 100 mg/kg/day (lower fetal weight, visceral variations and skeletal variations and malformations). Maternal NOEL = > 1000 mg/kg/day. ACCEPTABLE. (Kishiyama and Gee, 7/16/03).
US EPA (1993): Developmental NOEL = 100 mg/kg/day; maternal NOEL = 300 mg/kg/day (reduced weight gain at termination of study (possibly due to lower gravid uterine weight)).

TERATOLOGY, RABBIT

002 088734 Lemen, J. K. "Rabbit teratology Study with Biobor® JF." (Hazleton Laboratories America Incorporated, HLA Study No.182-131, July 11, 1990.) BIOBOR® JF, purity 100% (assumed), was administered by gavage at doses of 0 (corn oil), 25, 75, or 225 mg/kg to 17 pregnant New Zealand White Rabbits/group on days 7 through 19 of gestation. No evidence of maternal toxicity. Maternal NOEL = > 225 mg/kg/day. **Possible adverse effects (fetuses)** : mid and high-dose groups had skeletal variations related to incomplete ossification and variability in the number of ribs and presacral vertebrae [5th sternbrae unossified, absent sternbra(e), and 7th cervical rib(s)]. There was no dose-related increase in visceral or skeletal malformations. Developmental NOEL = 25 mg/kg/day. UNACCEPTABLE (rationale for dose selection was not stated). Upgradeable. (Kishiyama and Gee, 7/16/03).
US EPA (1993): Maternal NOEL = 225 mg/kg/day, Developmental NOEL = 25 mg/kg/day (ossification of sternbrae)

GENE MUTATION

** 004 114605 Lawlor, T.E. "Mutagenicity Test on Biobor® JF in the Ames *Salmonella*/Microsome Reverse Mutation Assay." (Hazleton Laboratories America, Inc., HLA Study No.: 10630-0-401, June 11, 1990) Biobar® JF (95% purity) was tested at concentrations of 0 (corn oil), 0.1, 0.5, 1, 5, 10, 50, and 100 µl/plate for mutagenicity using *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538 by the plate incorporation assay. There were triplicate plates per concentration with and without rat liver activation. There were two trials. No significant increase of revertants was reported with Biobor® exposure under study conditions. ACCEPTABLE. (Kishiyama and Gee, 7/22/03).

The RED of US EPA lists a study with mouse lymphoma that is not on file with the Department. The study is by Microbiological Associates, Lab number NO1-CP-41004, 1988.

CHROMOSOME EFFECTS

004 114604 Ivett, J. L. "Mutagenicity Test on Biobor® JF in the *In Vivo* Mouse Micronucleus Assay." (Hazleton Laboratories America, Incorporated, HLA Study No.: 10630-0-455, March 13, 1989.) Biobar® JF (lot HP 7322, purity not identified) was administered at doses of 0 (corn oil), 500, 2500, or 5000 mg/kg *via* a single gavage to five ICR mice/sex/group. Mice were sacrificed at 24, 48 or 72 hours post-dosing. One thousand polychromatic erythrocytes per animal were scored for micronuclei and the ratio of normochromatic erythrocytes to PCEs determined. The PCE value for high dose males (5000 mg/kg) was statistically significantly higher at 48 hours but considered by the author as a statistical anomaly due to the low micronucleus value in the control compared with the historical control range. Also, there was no time course for an effect. Females did not show any increase in micronuclei. UNACCEPTABLE (dosing material purity needs to be confirmed). Upgradeable. (Kishiyama and Gee, 7/22/03).

DNA DAMAGE

004 114606 Cifone, M. A. "Mutagenicity Test on Biobor® JF in the Rat Primary Hepatocyte Unscheduled DNA Synthesis Assay." (Hazleton Laboratories America, Inc., HLA Study No.: 10630-0-447, February 27, 1989.) Biobor® JF (lot # HP7322, purity not stated) was tested at

101 to 1010 µg/ml in Assay #2 and 50.6 to 380 µg/ml in a second assay for DNA damage by measuring UDS in primary rat hepatocytes *in vitro*. The first trial was not completed due to poor cell attachment. UDS was evaluated by autoradiography. There were triplicate coverslips per concentration in each trial with 50 cells scored per coverslip for a total of 150 cells per concentration. No significant changes in the nuclear labeling of rat primary hepatocytes. Summary data only were presented. UNACCEPTABLE (the results from individual cultures and the nuclear and cytoplasmic counts and test article purity were not included in the report). Upgradeable. (Kishiyama and Gee, 7/23/03).

MISCELLANEOUS

Subchronic, Rabbit dermal

005 114609 Lemen, J. K. "13-Week Dermal Toxicity Study in Rabbits with Biobor® JF." (Hazleton Laboratories America, Inc., HLA Study No. 182-133, December 26, 1989.) Biobor® JF (lot LH No. 24,064C, purity not given but assumed 100%) was administered at doses of 0, 105, 525, or 1050 mg/kg/day, 5 days/week for 13 weeks. Test material was applied undiluted to the dorsal skin of 10 New Zealand rabbits/sex/group under occluded wrap. The site of treatment application showed one or more signs of dermal irritation at all doses, including some in corn oil controls. Dermal NOEL <105 mg/kg/day. Hematocrit and hemoglobin levels were decreased for high dose females but not for males. There were no treatment-related effects on body weight, food consumption, clinical chemistry, ophthalmology or histopathology other than skin. Systemic NOEL for females = 525 mg/kg/day. UNACCEPTABLE. Upgradeable (confirmation of purity of test article) (Kishiyama and Gee, 7/24/03).