CALIFORNIA DEPARTMENT OF FOOD AND AGRICULTURE
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA

METHYL ISOBUTYL KETONE

SB 950 # 749[a], Tolerance # 51261

December 22, 1988

I. DATA GAP STATUS

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:	Data gap, inadequate study, no adverse effect indicated
Teratology, mouse:	Data gap, inadequate study, no adverse effect indicated

Gene mutation: Data gap, inadequate studies, no adverse effect indicated

Chromosome effects: Data gap, inadequate studies, no adverse effect indicated

DNA damage: Data gap, inadequate studies, no adverse effect indicated

Neurotoxicity: Not required at this time

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[a] Methyl isobutyl ketone is no longer registered in California as an active ingredient but is still contained in formulated products as an inert in products registered in California.

Toxicology one-liners are attached.

** indicates an acceptable study.
Bold face indicates a possible adverse effect.
File name: T881220, prepared by J. Gee. Record numbers in volume 001 rectified with Registration's Library listing.

II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

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

001 047194 "An evaluation of the teratogenic potential of methyl isobutyl ketone." (Bushy Run Research Center, 3/27/85) Methyl isobutyl ketone, 99.5%; given by inhalation days 6 - 15 of gestation, 6 hours per day, to Fischer 344 rats, 35 per group; whole-body exposure to 0 (air), 300, 1000 or 3000 ppm; nominal maternal NOEL = 1000 ppm (lower body

weight gain, clinical signs, decreased food consumption), developmental NOEL = 1000 ppm (lower fetal body weight); no treatment-related "malformations" reported; actual chamber concentration determined by sampling each hour; unacceptable (summary report with no individual data - full report should be submitted), no adverse developmental effect from summary data. Gee, 12/21/88.

TERATOLOGY, MOUSE

001 047195 "An evaluation of the teratogenic potential of methyl isobutyl ketone." (Bushy Run Research Center, 3/27/85) Methyl isobutyl ketone, 99.5%; given by inhalation days 6 - 15 of gestation, 6 hours per day, to CD-1 mice, 30 per group; whole-body exposure to 0 (air), 300, 1000 or 3000 ppm; nominal maternal NOEL = 1000 ppm (3 deaths at 3000 ppm, clinical signs); developmental NOEL = 1000 ppm (lower fetal body weight); no treatment-related "malformations" reported; actual chamber concentration determined by sampling each hour; unacceptable (summary report with no individual data - full report should be submitted), no adverse developmental effect from summary data. Gee, 12/21/88.

GENE MUTATION

001 047189 "Methyl isobutyl ketone (MIBK) - Mutagenicity studies: Gene mutation assay in Salmonella bacteria (Ames test)." (Microbiological Associates, [10/29/85] - record a summary prepared by Research and Environmental Health Division, Exxon, from actual report) Methyl isobutyl ketone, no purity, CAS #108-10-1; tested with Salmonella typhimurium strains TA1535, TA1537, TA1538, TA98 and TA100 with and without activation with Aroclor-induced Sprague-Dawley rat liver at 0 (DMSO), 0.04, 0.1, 0.4, 1 or 4 µl/plate, triplicate plates, repeat with TA1535 + S9; concentrations stated as based on a preliminary toxicity test but no data included in summary; table of data labeled with "MEK" - error?; no increase in reversion rate reported; full study on file at REHD should be submitted. Unacceptable (summary only). Gee, 12/20/88.

001 047190 "Methyl isobutyl ketone (MIBK) - Mutagenicity studies: Mouse lymphoma mutagenesis assay." (Microbiological Associates, [10/29/85] - date of summary document from Research and Environmental Health Division, Exxon) Methyl isobutyl ketone, no purity stated; tested with mouse lymphoma with and without S9 activation, incubated for 4 hours with 0 (DMSO), 0.32 to 4.2 µl/ml (10 concentrations) in trial 1; at 0, 0.6, 1.4, 2.1, 2.9 or 3.7 without activation and 0, 1.4, 1.9, 2.5, 3.0 or 3.4 with activation, duplicate cultures, in trial 2; assay repeated because of equivocal result without activation at the highest concentration in first trial; in second trial, mutation frequency increased significantly only when % total growth less than 10%; no biologically significant adverse effect. Unacceptable (summary only - the complete report on file at REHD should be submitted). Gee, 12/20/88.

CHROMOSOME EFFECTS

001 047192 "Methyl isobutyl ketone (MIBK) - Mutagenicity studies: Micronucleus cytogenetic assay in mice." (Microbiological Associates, MD, [10/29/85] - date of summary document from Research and Environmental Health Division, Exxon) Methyl isobutyl ketone, no purity stated; route of administration not stated - presumably oral gavage; tested with CD-1 mice, at 0 (corn oil) and 0.73 ml/kg (stated to be the LD_{20} determined from a preliminary test - no data); sacrificed 5/sex/group at 12, 24 and 48 hours; evaluated 1000 polychromatic erythrocytes per animal; proportion of PCE's per total erythrocytes reported; TEM as positive control; no increase in micronucleated PCE's reported at any sacrifice time; no change in ratio of PCE/NCE; unacceptable (summary only - full report should be submitted from REHD files). Gee, 12/21/88.

DNA DAMAGE

001 047191 "Methyl isobutyl ketone (MIBK) - Mutagenicity studies: Unscheduled DNA synthesis (UDS) in rat primary hepatocytes." (Microbiological Associates, [10/29/85] - date of summary document from Research and Environmental Health Division, Exxon) Methyl isobutyl

ketone, no purity stated; tested with primary hepatocytes from male Sprague-Dawley rats; preliminary cytotoxicity test indicated a 66% reduction in viability at 100 µl/ml; incubated for 18 hours with 0 (DMSO), 0.01, 0.1, 1, 10 or 100 µl/ml in triplicate; counted 100 cells following autoradiography; subtracted background of average of three nuclear-sized areas of cytoplasm; 10 and 100 µl/ml too toxic to evaluate; no increase in unscheduled DNA synthesis; unacceptable (summary only) - report on file at RHED should be submitted. Gee, 12/21/88.

001 047193 "Methyl isobutyl ketone (MIBK) - Mutagenicity studies: Transformation assay with Balb/3T3 mouse embryo cells." (Microbiological Associates, MD, [10/29/85] - date of summary document from Research and Environmental Healthe Division, Exxon) Methyl isobutyl ketone, no purity stated; tested for cell transformation with Balb/3T3 cells in two trials; with and without S9 activation; first trial: without activation at 0 (PBS), 2.4, 3.6 or 4.8 µl/ml, with activation at 0 (PBS), 1, 2 or 4 µl/ml, 2 hours incubation; second trial: without activation at 0, 4, 5, 6 or 7 µl/ml, with activation at 0, 2, 3, 4 or 5 µl/ml; MNNG and BaP as positive controls; 15 plates per concentration for foci and 3 for cytotoxicity; type II and type III foci reported; cytotoxicity at higher concentrations from decreased cloning efficiency; no consistent effect on transformation - no adverse effect reported; unacceptable (summary report - full report should be submitted from REHD files), possibly upgradeable. Gee, 12/21/88.

NEUROTOXICITY

No study on file for acute delayed neurotoxicity. Not required at this time.

SUBCHRONIC

001 No record number "A 14-week vapor inhalation toxicity study of methyl isobutyl ketone." (NASA, Summary of study written by Phillips et al. of multiple industries, 1986) Methyl isobutyl ketone, Exxon, 99%; Fischer 344 rats and $B6C3F_1$ mice, both sexes (6/sex/group

in probe study, 14/sex/group in main study) exposed by inhalation for 6 hours per day at 0 (air), 50, 250 or 1000 ppm (mean actual concentrations were 50, 252 and 1002 ppm); actual chamber content determined by gas chromatography of numerous samples; eye exam weekly; hematology, clinical chemistry and urinalysis on 10 rats/sex/dose; histopathology on rats and mice from control and high dose groups; the authors state no histopathology findings related to treatment other than an increase in hyaline droplets in kidneys of male rats - incidence was the same (including controls) but severity increased with dose and it was suggested in the report as possibly related to alpha-2U globulin rat-specific protein; authors stated NOEL = 50 ppm; summary with insufficient information for evaluation; unacceptable (summary report - full report should be submitted for evaluation with all histopathology findings and individual data.) Gee, 12/21/88.

SUMMARY AND/OR EVALUATION

001 047198 "Patty's industrial hygiene and toxicology: Methyl isobutyl ketone." Page 4747. No date. Summary of biologic effects from published literature. No neurological effects were found in long-term studies up to 11 months in dogs given methyl isobutyric ketone by subcutaneous injection. In rats, the kidney damage of hyaline droplet tubular nephrosis was stated to be reversible, even after 90 days of exposure. No worksheet. Gee, 12/22/88.