

CALIFORNIA DEPARTMENT OF FOOD AND AGRICULTURE
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA

PINE OIL

SB 950-321, Tolerance # 50250
Chemical # 000485

September 4, 1986
Revised February 23, 1989, July 3, 1990 and 1/12/98

I. DATA GAP STATUS

Subchronic rat:	No data gap, no adverse effect (dermal application)
Chronic rat:	Data gap, no study on file
Chronic dog:	Data gap, no study on file
Onco rat:	Data gap, no study on file
Onco mouse:	Data gap, no study on file
Repro rat:	Data gap, no study on file
Terato rat:	No data gap, no adverse effect
Terato rabbit:	Data gap, no study on file
Gene mutation:	No data gap, no adverse effect
Chromosome:	No data gap, no adverse effect
DNA damage:	No data gap, no adverse effect
Neurotox:	Not required at this time

Note, Toxicology one-liners are attached

** indicates acceptable study

Bold face indicates possible adverse effect

File name: T980112, revised 2/89, 7/90 and 1/12/98 by J. Gee

*****The question of use of the Tier system for antimicrobials has been raised in the determination of data requirements for pine oil.

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CHRONIC, RAT

No study on file.

CHRONIC, DOG

No study on file.

ONCOGENICITY, RAT

No study on file.

ONCOGENICITY, MOUSE

No study on file.

REPRODUCTION, RODENT

No study on file.

TERATOGENICITY, RAT

062 043029 (International Bio-Research, Inc. Germany, 11/77) Pine Oil 60, by gavage on days 6-15 at 0, 80, 200 or 500 ul/kg. MTD not reached, therefore maternal and developmental NOEL > 500 ul/kg. UNACCEPTABLE. Not upgradeable (MTD), no adverse effect. J. Parker, 9/3/86.

** 102, 109 068205, 071042, 071043 "Developmental Toxicity (Embryo/Fetal Toxicity and Teratogenic Potential) Study of Pine Oil Blend 1687 Administered Orally via Gavage to Crl:CD® (SD)BR Presumed Pregnant Rats." (Argus Research Laboratories, PA, Study CSMA 10-9, 1/27/88) Pine oil blend 1687 (see 071042 and 071043 in 50250-109 for composition); tested with Crl:CD® (SD)BR rats, 25 per group, at 0 (corn oil), 50, 600 or 1200 mg/kg/day by oral gavage, days 6 - 15 of gestation. Doses were selected based on a range-finding study; 6/25 deaths at 1200 mg/kg/day; dose-dependent increase in clinical signs during dosing of salivation, ungroomed coat, ataxia, alopecia, decreased motor activity, impaired righting reflexes; maternal NOEL = 50 mg/kg/day (decreased body weight gain, decreased food consumption primarily days 6 - 9 at 600 and 1200 mg/kg/day); developmental NOEL = 50 mg/kg/day (delayed development - marginal at 600 but significant at 1200 mg/kg/day; a number of other fetal effects at 1200 mg/kg/day in presence of overt maternal toxicity). **No adverse developmental effect.** ACCEPTABLE. Gee, 1/6/89.

TERATOGENICITY, RABBIT

No study on file.

GENE MUTATION

** 101, 109 068200, 071042, 071043 "CHO/HGPRT Mutation Assay in the Presence and Absence of Exogenous Metabolic Activation." (Microbiological Associates, T5366.332001, 9/1/87) CSMA 1687, pine oil blend, characterization in 071042 and 071043; tested with CHO/HGPRT Chinese hamster ovary cells for mutation to resistance to 6-thioguanine after 5 hours treatment with and without rat liver activation; without activation tested with untreated cultures, solvent (DMSO) controls and 100, 130, 170, 200 or 250 nl/ml, duplicate cultures; with activation, with untreated controls, solvent controls and 50, 100, 200, 300 or 400 nl/ml; repeat trials for both conditions; no evidence for an increase in mutation frequency to treatment levels resulting in reasonable cytotoxicity in at least one trial; ACCEPTABLE. Gee, 10/3 1/88.

** 173 157495 "Pine oil: *Salmonella typhimurium* reverse mutation assay" (S. Ferrante, Toxikon Corporation, Woburn, MA, Lab. Study # 94G-0332, 9/14/94) CSMA Pine Oil Blend 012494 (100%, Batch Ref. # 5558-012494) was tested with *Salmonella typhimurium* strains TA1535, TA1537, TA98, TA100 with and without activation by Aroclor 1254 induced rat liver homogenate activation system (S-9 mix), triplicate plates, for activated and nonactivated systems, single trial. Dose ranges: 0.1 - 10000 ug/plate, 65 hour incubation. No increase in reversion rate reported. No adverse effects indicated. **Acceptable.** (Miller, 11/25/97)

CHROMOSOMES

** 101 068201 "Micronucleus Cytogenetic Assay in Mice; Final Report." (Microbiological Associates, T5366.122, 9/1/87) Pine Oil Blend, CSMA 1687, characterization in 071042 and 071043; given to CD-1 mice by a single intraperitoneal injection; preliminary toxicity study with 5/sex/group at 0 (corn oil), 1000, 1300, 1600, 2000, 3000, 4000 or 5000 mg/kg, 10 ml/kg with all animals dying in the top three doses and at 1600 mg/kg; LD₅₀ approximately 1444 mg/kg; for micronucleus study, 15/sex/group were injected with 0, 116, 578 or 1155 mg/kg (80% of the LD50/7) with 5/sex/group sacrificed at 24, 48 or 72 hours; TEM as positive control; micronuclei per 1000 polychromatic erythrocytes and percent polychromatic erythrocytes per total erythrocytes were scored; 2/18 males and 3/18 females (three extra animals in high dose group as replacements) died before scheduled sacrifice; no adverse effect reported; ACCEPTABLE. Gee, 11/1/88.

DNA DAMAGE/OTHER

** 101 068202 "Unscheduled DNA Synthesis in Rat Primary Hepatocytes with a Confirmatory Assay." (Microbiological Associates, T5366.380016, 9/3/87) Pine Oil Blend, CSMA 1687, characterization in 109, #'s 071042 and 071043; tested at 0 (DMSO) and ten concentrations over a range of 0.0003 to 10 ml/ml, 18 - 20 hours, with male rat primary hepatocytes; two trials with nuclei from 0.0003, 0.001, 0.003, 0.01 and 0.03 ml/ml scored for grain counts by autoradiography - higher concentrations were toxic and test material immiscible at 1.0 and above; cytotoxicity measured by release of lactic acid dehydrogenase into the medium and by microscopic examination; scored 50 nuclei per each of three slides per concentration and results of parallel cytotoxicity assay included; net nuclear counts reported; no evidence of induction of unscheduled DNA synthesis; ACCEPTABLE. Gee, 11/1/88.

NEUROTOXICITY

Not required at this time.

SUPPLEMENTAL STUDIES

Subchronic dermal

** 103 (2 parts) 068206 "90-Day Dermal Toxicity Study in Rats with Pine Oil Blend CSMA 1687: Final Report." (WIL Research Laboratories, Project No. WIL-114006, 2/2/88) Pine Oil Blend CSMA 1687, tested neat on skin of Crl:CD BR rats, 10/sex/group at 0 (deionized water), 50, 113 or 226 mg/kg/day, 5 days per week, for 13 weeks; volumes applied were 0.24 ml water, 0.05, 0.12 or 0.24 ml pine oil blend; site of application was rotated over 4 quadrants to maintain the skin barrier; treated areas covered with gauze and animals fitted with a collar; systemic NOEL \geq 226 mg/kg/day, dermal NOEL < 50 mg/kg/day (desquamation, scabbing, erythema). The only microscopic finding at all doses was an increase in vacuolated macrophages containing basophilic ("tingable") nuclear debris in the thymus. No other findings. Composition in 109, # 071042. ACCEPTABLE. No adverse effect. Gee, 2/22/89.

043 002578 "Twenty day subacute toxicology study (albino rabbits)." (Bio-Toxicology Laboratories, 11/30/70) Pine-Sol, 30% pine oil, was tested by dermal applications to intact (male) skin and abraded (female) skin of albino rabbits, 1 per sex per dose group. Pine-Sol was applied at 1, 2, or 4 cc/kg over approximately 10% of the body for 5 days per week with a total of 20 applications. No information on the length of daily exposure or whether sites were occluded. **No effects reported** other than "faint scaliness" of treated skin. No effects on body weights, food consumption or gross necropsy findings. UNACCEPTABLE (inadequate number of animals, insufficient information). Gee, 7/3/90.