

CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA
METHYL ANTHRANILATE

Chemical Code # 3971 Document Processing Number (DPN) # 52037

Jan 10, 2014

DATA GAP STATUS

Chronic toxicity, rat:	No study on file ¹
Chronic toxicity, dog:	No study on file ¹
Oncogenicity, rat:	No study on file ¹
Oncogenicity, mouse:	No study on file ¹
Reproduction, rat:	No study on file ¹
Developmental toxicity, rat:	No study on file ¹
Developmental toxicity, rabbit:	No study on file ¹
Gene mutation:	No study on file ¹
Chromosome effects:	No study on file ¹
DNA damage:	No study on file ¹
Neurotoxicity:	No study on file ¹

¹ Methyl Anthranilate has been classified as a "biochemical" by CDPR. Therefore the US EPA toxicological data requirements for biochemicals apply. See discussion below. No further studies are required at this time to satisfy SB950 data requirements for Methyl Anthranilate.

Toxicology one-liners are attached.

All record numbers for the above study types through 219399 (Document No. 52037-0054) were examined. This includes all relevant studies indexed by DPR as of Jan 10, 2014.

In the 1-liners below:

 indicates an acceptable study.

Bold face indicates a possible adverse effect.

 ## indicates a study on file but not yet reviewed.

File name: t20140110. Created by Leung, Jan. 10, 2014

NOTE: The following symbols may be used in the Table of Contents which follows:

- ** = data adequately address FIFRA requirement
- † = study(ies) flagged as “possible adverse effect”
- (N/A) = study type not currently required

This record contains summaries of studies. Individual worksheets provide detailed assessment.

Table of Contents

METABOLISM AND PHARMACOKINETICS.....	3
SUBCHRONIC STUDIES (units of mg/kg/day unless specified).....	3
Oral toxicity, rat:.....	3
Oral toxicity, non-rodent:	3
Dermal toxicity, 21/28-day or 90-day:	3
CHRONIC STUDIES	3
Chronic, rat	3
Chronic, dog	4
Oncogenicity, rat	4
Oncogenicity, mouse	4
GENOTOXICITY.....	4
Bacterial reverse mutation assay	4
Mutagenicity: <i>In vitro</i> mammalian cell assay.....	4
Mutagenicity: <i>In vivo</i> cytogenetics.....	4
REPRODUCTIVE TOXICITY, RAT	4
DEVELOPMENTAL TOXICITY	5
Rat.....	5
Rabbit.....	5
NEUROTOXICITY	5
Acute neurotoxicity, rat	5
90-day neurotoxicity, rat.....	5
Developmental neurotoxicity, rat	5
Delayed neurotoxicity, hen.....	5
IMMUNOTOXICITY.....	5
ENDOCRINE DISRUPTOR STUDIES.....	5
SUPPLEMENTAL STUDIES	5

Note: Methyl anthranilate occurs naturally in a variety of flowers^{2,3} and fruits such as Concord grapes and other *Vitis labrusca* grapes, bergamot, black locust, champaca, gardenia, jasmine, lemon, mandarin orange, neroli, oranges, rue oil, strawberry, tuberose, wisteria. The active ingredient is exempt from the requirement of a tolerance in or on all food commodities (Federal Register, Vol. 67, No. 152, p. 51083-51088, 8/1/02). This exemption was based on the ubiquitous presence of methyl anthranilate in food, and its volatility and rapid breakdown in the environment and in the human gut. Methyl anthranilate is used as flavoring agent in candy, soft drinks, gums, and drugs. In addition, methyl anthranilate is general recognized as safe (GRAS) by the Food and Drug Administration (21 CFR § 182.60).

²Pesticide Science 47, 355-362, 1966

³Records of natural Products, 5:3, 202-207, 2011

TOXICOLOGY ONE-LINERS AND CONCLUSIONS:

METABOLISM AND PHARMACOKINETICS

There is no study of this type on file.

SUBCHRONIC STUDIES (units of mg/kg/day unless specified)

Oral toxicity, rat:

There is no study of this type on file.

Oral toxicity, non-rodent:

There is no study of this type on file.

Dermal toxicity, 21/28-day or 90-day:

There is no study of this type on file.

CHRONIC STUDIES

Chronic, rat

52037-0054 219399; "Bioassay of Anthranilic Acid for Possible Carcinogenicity" (Southern Research Institute, Birmingham, Alabama; DHEW Publication No. (NIH) 78-836; NCI-CG-TR-36; 1978). Anthranilic acid was administered in feed to 35 Fischer 344 rats/sex/dose at 15,000 or 30,000 ppm and 35 B6C3F1 mice/sex/dose at 25,000 or 50,000 ppm, 5 days per week for 78 weeks (observed for an additional 26-27 weeks). Matched controls: 15 rats and 15 mice of each

sex; pooled controls (for statistical evaluation); matched controls were combined with 15 untreated male and 15 untreated female animals of each species from a similar bioassay of another test chemical; except for the matched-control male mice, all surviving animals in the study were killed at 104-106 weeks; half of the matched-control male mice (accidentally killed at week 12) excluded from the report; remaining matched-control males died by week 94. Mean body weights of the low- and high-dose male and high-dose female rats were lower than those of the corresponding matched controls for the duration of the study; weights of the low-dose females were similar to those of the matched controls for the first 45 weeks, after which they declined slightly; weights of the low-dose male mice were similar to those of the matched controls; those of the high-dose males and of the low- and high-dose females were slightly lower. Survival of both treated and matched-control groups of rats of both sexes was high; survival of treated mice of both sexes and of female matched controls was lower than that of the rats. In rats, tumor incidence showed no statistically significant increase when compared with controls; in mice, neoplasms were found that are common to the strain (*e.g.*, hepatocellular adenoma or carcinoma), with no significant increase in treated groups compared to controls. Supplemental. Kellner, 9/7/05.

Chronic, dog

There is no study of this type on file.

Oncogenicity, rat

(Record 219399 in the above "Chronic, rat" section contains oncogenicity results.)

Oncogenicity, mouse

There is no study of this type on file.

GENOTOXICITY

Bacterial reverse mutation assay

There is no reviewable study of this type on file.

Mutagenicity: *In vitro* mammalian cell assay

There is no reviewable study of this type on file.

Mutagenicity: *In vivo* cytogenetics

There is no reviewable study of this type on file.

REPRODUCTIVE TOXICITY, RAT

There is no study of this type on file.

DEVELOPMENTAL TOXICITY

Rat

There is no study of this type on file.

Rabbit

There is no study of this type on file.

NEUROTOXICITY

Acute neurotoxicity, rat

There is no study of this type on file.

90-day neurotoxicity, rat

There is no study of this type on file.

Developmental neurotoxicity, rat

There is no study of this type on file.

Delayed neurotoxicity, hen

There is no study of this type on file.

IMMUNOTOXICITY

There is no study of this type on file.

ENDOCRINE DISRUPTOR STUDIES

There is no study of this type on file.

SUPPLEMENTAL STUDIES

Not applicable.
