CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
HUMAN HEALTH ASSESSMENT BRANCH

SUMMARY OF TOXICOLOGY DATA
Tagetes Oil

Chemical Code # 6196, Document Processing Number (DPN) # 53292

11 February 2015

DATA GAP STATUS

Chronic toxicity, rat:	No study submitted, not required at this time[1]
Chronic toxicity, dog:	No study submitted, not required at this time[1]
Oncogenicity, rat:	No study submitted, not required at this time[1]
Oncogenicity, mouse:	No study submitted, not required at this time[1]
Reproduction, rat:	No study submitted, not required at this time[1]
Developmental toxicity, rat:	No study submitted, not required at this time[1]
Developmental toxicity, rabbit:	No study submitted, not required at this time[1]
Gene mutation:	No data gap, no adverse effect
Chromosome effects:	No study submitted, not required at this time[1]
DNA damage:	No study submitted, not required at this time[1]
Neurotoxicity:	No study submitted, not required at this time[1]

Toxicology one-liners are attached.

All record numbers for the above study types through 282045 (53292-0028) were examined.
In the 1-liners below:
indicates an acceptable study. **Bold face indicates a possible adverse effect.
File name: T150211 prepared by H. Green.

[1]Toxicology data for Tagetes Oil have been submitted and reviewed as a biochemical pesticide. These studies are not required at this time. The active ingredient, Tagetes Oil, is used as a natural flavoring agent and is incorporated into some cosmetics including shampoos, soaps, and lotions.

This record contains summaries of studies. Individual worksheets may be useful for detailed assessment.

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METABOLISM AND PHARMACOKINETICS

Not required at this time.

GUIDELINE ACUTE STUDIES ON ACTIVE INGREDIENT

Acute oral toxicity, rat

**53292-0001, 0020 278002, 278037, "Acute Oral Toxicity in the Rat (Up and Down Procedure)" (Arcelin, G., Harlan Laboratories Ltd, Fullinsdorf, Switzerland, Harlan Laboratories Study C36105, 08/05/2009). 870.1100. Tagetes oil (Batch Number X25902, purity not provided), formulated in PEG 300, was administered as a single dose by oral gavage to 3 HanRcc:WIST (SPF) female rats at a dose level of 5000 mg/kg. No animals died during a 14-day observation period. Ruffled fur, hunched posture, and sedation in all animals and almost completely closed eyes in one animal were observed after exposure with all signs clearing in all animals by test day 8. Necropsy revealed no macroscopic findings. Reported LD_{50} (F) > 5000 mg/kg. Originally reviewed as Toxicity Category not determined. Unacceptable but possibly upgradable with the submission of the purity of the test article. (Corlett, 09/03/2014). A number of components make up Tagetes oil at various percentages based on growing conditions and processing techniques of the *Tagetes minuta* plant (common names include Mexican marigold, Aztec marigold, and muster John Henry) it is extracted from. The components and their general ranges are limonene (2.9% to 49.2%), tagetone (6.2% to 13.4%), dihydrotagetone (13.7% to 21.4%), (E)-ocimenone (1.8% to 13.3%), (Z)-ocimenone (3.7% to 6.1%), ocimene (7.4% to 42.2%), and α-terpineol (7.4% to 20.8%) (See record 278002). Batch No. X25902 contained 27.1% ocimene. Based on correspondence with the registrant, DPR accepts that the sum of the components constitutes Tagetes oil at 100%. The study is upgraded to acceptable with LD_{50} (F) > 5000 mg/kg. Toxicity category IV. (Green, 1/6/15).

Acute dermal toxicity

** 53292-0001, 0018 278002, 278035, "Acute Dermal Toxicity Study in Rats" (Arcelin, G., Harlan Laboratories Ltd, Fullinsdorf, Switzerland, Harlan Laboratories Study C36116, 08/05/2009). 870.1200. Tagetes oil (Batch Number X25902, purity not provided), formulated in PEG 300, was applied to the clipped skin of the back of 5 HsdHan:WIST (SPF) rats per sex per dose at a dose level of 2000 mg/kg for 24 hours using a semi-occlusive dressing . No animals died during a 14-day observation period. No clinical signs were observed. Very slight erythema was observed in all animals at the test site after removal of the dressings. All signs of erythema cleared in all test animals by test day 10. Scaling of the skin at the test site was observed in 2 males and 2 females, persisting in the females through test day 15. Scabs at the test site were observed in 1 female on test day 10 through test day 15. Necropsy revealed no macroscopic findings. Originally reviewed as reported LD_{50} (M/F) > 2000 mg/kg. Toxicity Category not determined. **Unacceptable but possibly upgradable** with the submission of the purity of the test article. (Corlett, 09/03/2014). A number of components make up Tagetes oil at various percentages based on growing conditions and processing techniques of the *Tagetes minuta* plant (common names include Mexican marigold, Aztec marigold, and muster John Henry) it is extracted from. The components and their general ranges are limonene (2.9% to 49.2%), tagetone (6.2% to 13.4%), dihydrotagetone (13.7% to 21.4%), (E)-ocimenone (1.8% to 13.3%), (Z)-ocimenone (3.7% to 6.1%), ocimene (7.4% to 42.2%), and α-terpineol (7.4% to 20.8%) (See record 278002). Batch No. X25902 contained 27.1% ocimene. Based on correspondence with the registrant, DPR accepts that the sum of the components constitutes Tagetes oil at 100%. The

study is upgraded to acceptable with LD_{50} (M & F) > 2000 mg/kg. Toxicity category III. (Green, 1/6/15).

Acute inhalation toxicity, rat

**53292-0001, 0028 278002, 282044, "Acute Inhalation Toxicity Study in Rats," (A. Doig, Stillmeadow, Inc., Sugar Land, TX, Laboratory Study No. 14506-10, December 15, 2010). Five Sprague-Dawley rats per sex were exposed to Tagetes oil (100%) for 4 hours by nose-only inhalation at 5.20 mg/l analytical (with mean mass median aerodynamic diameter (MMAD) of 2.9 um and a mean geometric standard deviation (GSD) of 5.0) followed by a 14 day observation period. All animals survived to the end of the 14-day observation period and gained bodyweight. Decreased activity and piloerection were noted in all animals from 4.5 hours to day 2 post-treatment. All animals appeared normal from days 3 to 14 post-treatment. No treatment-related changes were noted at necropsy. LC_{50} (M & F) > 5.20 mg/l. Toxicity category IV. Acceptable. (Green, 1/6/15).

Primary eye irritation, rabbit

53292-0001, 0019 278002, 278036; "Primary Eye Irritation Study in Rabbits" (Arcelin, G., Harlan Laboratories Ltd, Fullinsdorf, Switzerland, Harlan Laboratories Study C36138, 09/17/2009). 870.2400. 0.1 ml of Tagetes oil (Batch Number X25902, purity not provided) was placed into the conjunctival sac of one eye of each of 3 New Zealand White rabbits. No corneal opacity or iritis was observed. Grade 1 conjunctival redness was observed in all 3 treated eyes 24 hours after treatment with all signs of eye irritation clearing in all treated eyes 48 hours after treatment. Originally reviewed as Toxicity Category not determined. **Unacceptable but possibly upgradable with the submission of the purity of the test article. (Corlett, 09/03/2014). A number of components make up Tagetes oil at various percentages based on growing conditions and processing techniques of the *Tagetes minuta* plant (common names include Mexican marigold, Aztec marigold, and muster John Henry) it is extracted from. The components and their general ranges are limonene (2.9% to 49.2%), tagetone (6.2% to 13.4%), dihydrotagetone (13.7% to 21.4%), (E)-ocimenone (1.8% to 13.3%), (Z)-ocimenone (3.7% to 6.1%), ocimene (7.4% to 42.2%), and α-terpineol (7.4% to 20.8%) (See record 278002). Batch No. X25902 contained 27.1% ocimene. Based on correspondence with the registrant, DPR accepts that the sum of the components constitutes Tagetes oil at 100%. The study is upgraded to acceptable with Toxicity category IV. (Green, 1/7/15).

Primary dermal irritation

**53292-0001, 0016 278002, 278033; "Primary Skin Irritation Study in Rabbits (4-Hour Semi-Occlusive Application)" (Arcelin, G., Harlan Laboratories Ltd, Fullinsdorf, Switzerland, Harlan Laboratories Study C36127, 08/05/2009). 870.2500. 0.5 ml of Tagetes oil (Batch Number X25902, purity not provided) was placed onto a gauze patch and applied to the clipped left flank of each of 3 New Zealand White rabbits (held in contact by means of a semi-occlusive dressing) for 4 hours. Grade 1 edema was observed at the test site in all 3 animals 1 hour after patch removal with all signs of edema clearing in all animals 24 hours after patch removal. Grade 2 erythema observed at the test site in all 3 animals 1 hour, 24 hours, and 48 hours after patch removal; grade 2 erythema was observed in 2 animals and grade 1 erythema was observed in 1

animal 72 hour after patch removal and grade 1 erythema was observed in 1 animal 7 days after patch removal with all signs of erythema clearing in all animals 10 days after patch removal. Originally reviewed as Toxicity Category not determined. **Unacceptable but possibly upgradable** with the submission of the purity of the test article. (Corlett, 09/03/2014). A number of components make up Tagetes oil at various percentages based on growing conditions and processing techniques of the *Tagetes minuta* plant (common names include Mexican marigold, Aztec marigold, and muster John Henry) it is extracted from. The components and their general ranges are limonene (2.9% to 49.2%), tagetone (6.2% to 13.4%), dihydrotagetone (13.7% to 21.4%), (E)-ocimenone (1.8% to 13.3%), (Z)-ocimenone (3.7% to 6.1%), ocimene (7.4% to 42.2%), and α-terpineol (7.4% to 20.8%) (See record 278002). Batch No. X25902 contained 27.1% ocimene. Based on correspondence with the registrant, DPR accepts that the sum of the components constitutes Tagetes oil at 100%. The study is upgraded to acceptable with Toxicity category III. (Green, 1/7/15).

Dermal sensitization

53292-0001, 00017 278002, 278034; "Contact Hypersensitivity in Albino Guinea Pigs, Buehler Test" (Arcelin, G., Harlan Laboratories Ltd., Fullinsdorf, Switzerland , Harlan Laboratories Study C36847, 08/05/2009). 870.2600. The Buehler method was used to assess the skin sensitization potential of Tagetes oil (Batch Number X25902, purity not provided). 20 albino Dunkin Hartley (CRL:(HA)BR) guinea pigs were treated with the dosing material. For induction, 0.5 ml of the undiluted test material was applied to the shaved left shoulder region of each animal for 6 hours, once per week for 3 weeks (days 1, 8, and 15) using a Hill Top Chamber. On day 29, a challenge dose of 0.5 ml of a 1% concentration of the test material in PEG 300 material was applied to the shaved left back/side of each animal for 6 hours in the same manner as during the induction phase. A concurrent vehicle control group consisting of 10 males and 10 females was also included in the study. The positive control was functional. Observations after the removal of the challenge phase patches revealed no erythema at any treatment site. **The results of the study indicate that the test material is not a sensitizer when using this modified version of the method of Buehler. Originally reviewed as **Unacceptable but possibly upgradable** with the submission of the purity of the test article. (Corlett, 09/03/2014). A number of components make up Tagetes oil at various percentages based on growing conditions and processing techniques of the *Tagetes minuta* plant (common names include Mexican marigold, Aztec marigold, and muster John Henry) it is extracted from. The components and their general ranges are limonene (2.9% to 49.2%), tagetone (6.2% to 13.4%), dihydrotagetone (13.7% to 21.4%), (E)-ocimenone (1.8% to 13.3%), (Z)-ocimenone (3.7% to 6.1%), ocimene (7.4% to 42.2%), and α-terpineol (7.4% to 20.8%) (See record 278002). Batch No. X25902 contained 27.1% ocimene. Based on correspondence with the registrant, DPR accepts that the sum of the components constitutes Tagetes oil at 100%. The study is upgraded to acceptable. (Green, 1/7/15).

SUBCHRONIC STUDIES

Not required at this time.

CHRONIC STUDIES

Not required at this time.

GENOTOXICITY

Bacterial reverse mutation assay

**53292-0027 280242, "Tagetes Oil Bacterial Reverse Mutation Test, Final Report," (K. May, Huntingdon Life Sciences, Eye Research Centre, Eye, Suffolk, England, Project ID.GWZ0002, November 26, 2010). Triplicate cultures of *Salmonella typhimurium* strains TA98, TA100, TA1535, and TA1537 and *Escherichia coli* strain WP2 *uvr*A were exposed to Tagetes oil (100%), in the presence and absence of rat liver S9 mix, by direct plate incorporation for 72 hours at 5, 15, 50, 150, 500, 1500, and 5000 µg/plate in the first trial and at 50, 150, 500, 1500, and 5000 µg/plate in the second trial. There was no increase in the number of revertants per plate in either trial compared to the solvent controls. Positive controls were functional. No adverse effect. Acceptable. (Green and Leung, 10/23/14).

Mutagenicity: *In vitro* mammalian cell assay

Not required at this time.

Mutagenicity: *In vivo* cytogenetics

Not required at this time.

REPRODUCTIVE TOXICITY, RAT

Not required at this time.

DEVELOPMENTAL TOXICITY

Rat and Rabbit

Not required at this time.

NEUROTOXICITY

Not required at this time.

IMMUNOTOXICITY

Not required at this time.