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

SUMMARY OF TOXICOLOGY DATA
ACTIVE INGREDIENT 1, 2-Octanediol

Chemical Code # 6243, Document Processing Number (DPN) # 53338
SB 950 # None assigned
02/26/2016

DATA GAP STATUS

Chronic toxicity, rat:	No study required at this time[1]
Chronic toxicity, dog:	No study required at this time[1]
Oncogenicity, rat:	No study required at this time[1]
Oncogenicity, mouse:	No study required at this time[1]
Reproduction, rat:	No study required at this time[1]
Developmental toxicity, rat:	No data gap, no adverse effects
Developmental toxicity, rabbit:	No study required at this time[1]
Gene mutation:	No data gap, no adverse effects
Chromosome effects:	No data gap, no adverse effects
DNA damage:	No study required at this time[1]
Neurotoxicity:	No study required at this time[1]

[1]1, 2-Octanediol has been classified as a "biochemical" for purposes of toxicological data requirements by US EPA. No further studies are required at this time to satisfy SB950 requirements for 1, 2-Octanediol.

Toxicology one-liners are attached.

All record numbers for the above study types through 287068 (Document No. 53338-0007) were examined. This includes all relevant studies indexed by DPR as of 02/26/2016.

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:T20160226
Prepared by John Corlett, 02/26/2016

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 may be useful for detailed assessment.

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METABOLISM AND PHARMACOKINETICS

No study required at this time.

GUIDELINE ACUTE STUDIES ON ACTIVE INGREDIENT

Acute oral toxicity, rat

0003; 287049; "ADEKANOL OG: Acute Oral Toxicity (Limit Test) in the Rat" (Driscoll, R., Safepharm Laboratories Limited, Derby, UK, SPL Project Number: 744/048, 03/19/1999). 870.1100. ADEKANOL OG (Batch number 10238, purity = 98.5%) was suspended in arachis oil and administered once by gavage to 5 Sprague-Dawley CD (Crl:CD BR) rats per sex per dose at a dose level of 2000 mg/kg. No mortalities occurred. Hunched posture, lethargy, ataxia, decreased respiratory rate, and labored respiration were observed in all animals 4 hours after dosing with all signs clearing in all animals 2 days after dosing. Necropsy revealed no macroscopic abnormalities. LD_{50} (M/F) > 2000 mg/kg. Toxicity Category III. **Acceptable**. (Corlett, 12/15/2015)

Acute dermal toxicity

0003; 287050; "Acute Dermal Toxicity (Limit Test) with 1, 2 Octanediol" (Takawale, P., BSL Bioservice, Scientific Laboratories GmbH, Planegg, Germany, BSL Bioserve Study No. 140947, 04/23/2014). 870.1200. 1, 2 Octanediol (Batch No. 10133, purity = 98.5%), moistened with sterile water, was applied to the clipped dorsal skin of 5 Wistar (Crl:WI (Han) rats per sex per dose for 24 hours with the test article held in contact with the skin with a gauze dressing. No mortalities occurred. No signs of systemic toxicity were observed in any test animal. Grade 1 erythema was observed at the test site in all animals on test day 2 and in one male test animal on test day 3 with all signs of skin irritation clearing in all test animals on test day 4. Necropsy

revealed no specific macroscopic findings. LD_{50} (M/F) > 2000 mg/kg. Toxicity Category III. **Acceptable**. (Corlett, 12/04/2015)

Acute inhalation toxicity, rat

0003; 287051; "1, 2 Octanediol: Acute Inhalation Toxicity in Rats" (Merrill, D., Product Safety Labs, Dayton, NJ, Laboratory Study Number 37940, 04/14/2014). 870.1300. 1, 2 Octanediol (Batch No. 10133, purity = 98.5%) was aerosolized (while wrapped in foil to protect it from light and kept in a 45˚C water bath) and administered in a nose-only manner to 5 albino Sprague-Dawley derived rats per sex per dose at dose levels (mean gravimetric concentration) of 2.08 (males only) and 5.04 mg/L (with average MMADs (GSDs) of 2.11 (2.06) and 2.43 (2.13) µm, respectively) for 4 hours. Mortalities occurred as follows- males: 0/5, 2/5, respectively; females: 1/5 (5 males and 5 females were initially dosed with 5.04 mg/L and after the results were analyzed, 5 additional males were dosed with 2.08 mg/L). Clinical signs observed during the 14-day observation period following exposure included irregular respiration, hypoactivity, moist rales, ano-genital staining, and alopecia with all clinical signs clearing in all surviving animals by day 5 except for alopecia (head) in one female that persisted throughout the study. Necropsy on the mortalities revealed extremely red lungs; necropsy on the surviving animals revealed no gross abnormalities. 2.08 mg/L < LC_{50} (M)< 5.04 mg/L; LC_{50} (F) > 5.04 mg/L. Toxicity Category III. **Acceptable**. (Corlett, 12/07/2015)

Primary eye irritation, rabbit

0003; 287052; "Screening for the Eye Irritancy Potential Using the Bovine Corneal Opacity and Permeability Assay with 1, 2 Octanediol " (Schmitz, R., BSL Bioservice, Scientific Laboratories GmbH, Planegg, Germany, BSL Bioserve Study No. 135566A, 02/19/2014). 1, 2 Octanediol (Batch No. 10133, purity = 98.5%) was tested using the Bovine Corneal Opacity and Permeability Assay (BCOP). The test article, a white solid, was suspended in physiological saline (0.9% NaCl) for a 20% concentration. Nine bovine corneas, obtained as a by-product from freshly slaughtered animals, were mounted in special holders and exposed to the test article, and negative and positive control materials (3 corneas per substance). An aliquot of 750 uL of the test article substance, positive control, or negative control was introduced into the anterior chamber of the each holder and incubated at 32 ± 1°C for 4 hours ± 5 minutes. Based on changes in corneal opacity and permeability (relative to the control corneas), an *in vitro* irritation score of 63.32 was determined for the test article. Toxicity Category I eye irritation indicated. **Supplemental study.** (Corlett, 12/09/2015)

Primary dermal irritation

0003; 287053; "Acute Dermal Irritation/Corrosion with 1, 2 Octanediol" (Schmid, S., BSL Bioservice, Scientific Laboratories GmbH, Planegg, Germany, BSL Bioserve Study No. 140946, 06/25/2014). 870.2500. 0.5 g of 1, 2 Octanediol (Batch No. 10133, purity = 98.5%), moistened with sterile water, was applied to the clipped dorsal skin of 3 New Zealand White rabbits for 4 hours covered with a semi-occlusive dressing. Grade 1 erythema was observed in all 3 animals 1 hour, 48 hours, and 72 hours after patch removal, persisting in all 3 animals 4 and 5 days after patch removal, persisting in 2 animals 6, 7 and 8 days after patch removal, and clearing in all animals 9 days after patch removal. Grade 2 edema was observed in 2 animals 1 hour after patch removal, decreasing to grade 1 in 2 animals 48 hours, 72 hours, 4 days, and 5

days after patch removal with grade 1 edema persisting in 1 animal 6, 7, and 8 days after patch removal, and clearing in all animals 9 days after patch removal. Toxicity Category III. **Acceptable**. (Corlett, 12/07/2015)

Dermal sensitization

0003; 287054; "Test for Sensitisation (Guinea Pig Maximisation Test) with 1, 2 Octanediol" (Schmid, S., BSL Bioservice, Scientific Laboratories GmbH, Planegg, Germany, BSL Study Number: 140945, 05/27/2014). 870.2600. The guinea pig maximization test was used to assess the potential of 1, 2 Octanediol (Batch No. 10133, purity = 98.5%) to elicit delayed contact hypersensitivity in the guinea pig. 10 **C**rl:HA guinea pigs were treated with the test material at induction (intradermal injections followed by a topical application 1 week later) and at challenge (a topical application approximately 2 weeks after the topical induction). A concurrent negative control group consisting of a group of 5 animals was also included in the study. The control animals were treated identically to the test animals, except that during induction, the test material was replaced with the vehicles (0.9% NaCl and vaseline). The positive control was functional. The challenge sites were examined for skin reactions 24 and 48 hours after patch removal; no positive reactions were observed in the treatment group or in the control group. **The results of the study indicate that the test material is not a sensitizer when using the maximization test. Acceptable.** (Corlett, 12/10/2015)

SUBCHRONIC STUDIES

Oral toxicity, rat (28-Day):

0004; 287055; "Dermosoft Octiol: 28-Day Oral Toxicity (Gavage) Study in the Wistar Rat" (Braun, W.H. et al., RCC Ltd, Toxicology Operational Unit, Itingen, Switzerland, RCC Study Number 850714, 02/13/2004). 870.3050. Dermosoft Octiol (Batch number 10162, purity = 99.4%) was mixed with PEG 300 and administered by gavage daily for 28 days to 5 SPF-bred Wistar rats per sex per dose at dose levels of 0 (PEG 300 only), 50, 300, and 1000 mg/kg/day. No treatment-related mortalities occurred. No treatment-related clinical signs were observed during the daily cage-side observations or during the weekly detailed observations. No clinical signs were observed during the functional observational battery performed during week 4. A possible decrease in motor activity in both sexes at 1000 mg/kg/day during week 4 was observed. No treatment-related effects on mean body weight or mean food consumption were observed. Hematological and clinical biochemistry investigations revealed no treatment-related effects. Treatment-related increases in mean relative liver and kidney weights were observed in males and in females at 1000 mg/kg/day (female liver weight not statistically significant). Macroscopic examination revealed no treatment-related gross lesions. Microscopic examination revealed treatment-related minimal hyperkeratosis (parakeratotic) of the stomach (pars non-glandularis) in both sexes at 1000 mg/kg/day and epithelial hyperplasia of the stomach (pars non-glandularis) in males (minimal) and females (minimal to slight) at 1000 mg/kg/day. **No adverse effects**. NOEL (M/F)= 300 mg/kg/day, based on decreased motor activity, increased mean relative liver and kidney weights, and hyperkeratosis and epithelial hyperplasia of the stomach (pars non-glandularis). **Acceptable.** (Corlett and Leung, 01/05/2016)

Oral toxicity, rat (90-Day):

0005; 287056; "90-Day Repeated Oral Toxicity Study in Wistar Rats with 1, 2-Octanediol" (Takawale, P., BSL Bioservice Scientific Laboratories GmbH, Planegg, Germany, Laboratory Project Identification 135052, 07/09/2014). 870.3100. 1, 2-Octanediol (Batch number 10133, purity = 98.5%) was dissolved in sterile water and administered at a single dose by gavage daily for 90 days to 10 Wistar rats per sex per dose at dose levels of 0 (sterile water only), 50, 150, or 300 mg/kg/day. One male at 150 mg/kg/day died on day 40 (not considered treatment-related) and 2 females at 600 mg/kg/day were sacrificed for animal welfare reasons, one on day 20 and the other on day 60. Treatment-related salivation, abnormal breathing, piloerection, and moving of bedding were observed at 150 and 300 mg/kg/day in both sexes during the daily clinical observations. No treatment-related clinical signs were observed during the weekly detailed observations. No effects were observed during the functional observational battery performed during the last week of treatment. No treatment-related effects on mean body weight or mean food consumption were observed. Hematological, clinical biochemistry, and urinalysis investigations revealed no treatment-related effects. No treatment-related effects on the mean absolute or mean relative organ weights were observed. Macroscopic examination revealed no treatment-related gross lesions. Microscopic examination revealed no treatment-related effects. **No adverse effects**. NOEL (M/F)= 50 mg/kg/day, based on salivation, abnormal breathing, piloerection, and moving of bedding observed during daily clinical observations. **Acceptable.** (Corlett and Leung, 01/12/2016)

Oral toxicity, non-rodent:

No study required at this time.

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

No study required at this time.

CHRONIC STUDIES

Chronic, rat

No study required at this time.

Chronic, dog

No study required at this time.

Oncogenicity, rat

No study required at this time.

Oncogenicity, mouse

No study required at this time.

GENOTOXICITY

Bacterial reverse mutation assay**

** 0006, 287058; "Reverse Mutation Assay "Ames Test" Using *Salmonella typhimurium* and *Escherichia coli* (Pre-Incubation method)" (Thompson, P.W., Safepharm Laboratories Limited, Derby, UK, SPL Project Number: 744/047, 02/01/1999). 870.5100. Triplicate cultures of *S. typhimurium* strains TA1535, TA1537, TA98, and TA100 and of *Escherichia coli* strain WP2uvrA- were pre-incubated for 20 minutes at 37°C with Adekanol OG (Batch number 10238, purity = 98%), in the presence and absence of S9 rat liver fraction metabolic activation at 0 (DMSO), 5, 15, 50, 150, 500, 1500, and 5000 ug/plate. This was followed by plating and further incubation for 48 hours at 37°C. Two experiments were conducted in this manner. Positive controls were functional. There was no treatment-related increase in mutation frequency when compared to the negative (DMSO) control. Negative results indicate that under these test conditions the test article is not mutagenic in these tested strains. **No adverse effects indicated. Acceptable.** (Corlett and Leung, 01/29/2016)

Mutagenicity: *In vitro* mammalian cell assay**

** 0006, 287060; "Gene Mutation Assay in Chinese Hamster V79 Cells *In Vitro* (V79/HPRT) with Dermasoft Octiol" (Wollny, H.-E., Harlan Cytotest Cell Research GmbH, Rossdorf, Germany, Study Number 1229000, 04/22/2009). 870.5300. Cultures of the Chinese hamster V79 cell line (HPRT locus) were treated with Dermasoft Octiol (Batch No. 10268, purity = 98.8%) in 2 complete main experiments (each with and without exogenous Wistar rat liver S9 metabolic activation) using 2 parallel cultures each. In the first experiment, the cells were treated for 4 hours at concentrations of 0 (vehicle only, DMSO), 11.6, 23.1, 46.3, 92.5, and 185 ug/ml without S9 metabolic activation and at concentrations of 0, 92.5, 185, 370, and 740 ug/ml with S9 metabolic activation. In the second experiment, the cells were treated for 4 hours and 24 hours, activated and non-activated, respectively, at concentrations of 0, 92.5, 185.0, 370.0, 555.0, and 740.0 ug/ml. Positive controls of ethylmethane sulphonate (non-activated) and 7, 12-dimethylbenz(a)anthracene (activated) were used in each experiment. Following an expression time of 7 days, the cells were treated with 6-thioguanine. The positive controls were functional. No treatment-related effects were observed in the treated cells. No evidence of mutagenic effects was observed in this mammalian forward mutation system. **No adverse effects indicated. Acceptable.** (Corlett and Leung, 02/09/2016)

Mutagenicity: *In vitro* cytogenetics**

** 0006, 287059; "*In vitro* Chromosome Aberration Test of ADENKA NOL OG Using Mammalian Cultured Cells" (Zheng, M.-S., Biotoxtech Co., Ltd., Ochang-eup, Korea, Laboratory Project Identification J07019, 05/26/2007). 870.5375. Duplicate cultures of Chinese hamster lung cells (CHL/IU) were treated with ADEKA NOL OG (Lot No. 10196, purity > 98%) in 3 separate tests. In 2 of the tests, the cell cultures were treated with the test article for 6 hours at dose levels of 0 (DMSO, the solvent control), 175, 350, and 700 ug/ml, in one of the tests in the absence of S9 rat liver metabolic activation and in the other test in the presence of metabolic activation. In the 3rd test, the cell cultures were treated with the test article for 24

hours at dose levels of 0, 45, 90, and 180 ug/ml in the absence of metabolic activation. 2 hours prior to harvesting the cells, the cultures were treated with Colcemide to arrest the cells in metaphase. The positive controls were functional. No dose-related chromosomal aberrations were observed. The results of this study indicate that under these test conditions, the test article does not induce chromosomal aberrations in cultured mammalian somatic cells. **No adverse effects indicated. Acceptable.** (Corlett and Leung, 02/03/2016)

REPRODUCTIVE TOXICITY, RAT

No study required at this time.

DEVELOPMENTAL TOXICITY

Rat**

** 0006; 287057; "Prenatal Developmental Toxicity Study of 71868 in Wistar Rats by Oral Route " (Ramesh, E., Department of Safety Assessment, Advinus Therapeutics Limited, Bangalore, India, Study No. G8505, 07/05/2013). 870.3700. 71868 (Dermosoft Octiol) (Batch-No.: 10122, purity = 98.6%), suspended in PEG 300, was administered orally once daily by gavage to 24 Crl:CD (SD) mated female rats at doses levels of 0 (PEG 300 only), 150, 300, or 1000 mg/kg/day from gestation day 5 to gestation day 19. No mortalities occurred during the study. No clinical signs were observed at any dose level during the study. A treatment-related decrease in mean dam gravid uterus weight was observed at 300 and 1000 mg/kg/day. No treatment-related effects on fetus viability and post-implantation loss were observed. A treatment-related decrease in mean fetal body weight was observed at 1000 mg/kg/day. Visceral examinations of selected fetuses revealed no treatment-related abnormalities. Examination of the fetal skeletal structures revealed a treatment-related increased incidence of an accessory rib (#14) in fetuses at 1000 mg/kg/day. **No adverse effects. Maternal NOEL:** 150 mg/kg/day (based on decreased gravid uterine weight); **Developmental NOEL:** 300 mg/kg/day (based on a decrease in mean fetal body weight and an increased incidence of an accessory rib (#14)). **Acceptable.** (Corlett and Leung, 01/27/2016)

Rabbit

No study required at this time.

NEUROTOXICITY

Acute neurotoxicity, rat

No study required at this time.

90-day neurotoxicity, rat

No study required at this time.

Developmental neurotoxicity, rat

No study required at this time.

Delayed neurotoxicity, hen

No study required at this time.

IMMUNOTOXICITY

No study required at this time

ENDOCRINE DISRUPTOR STUDIES

No study required at this time.

SUPPLEMENTAL STUDIES

None submitted.