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

SUMMARY OF TOXICOLOGY DATA
ALPHA-CYPERMETHRIN

Chemical Code # 6131, **Document Processing Number (DPN)** # 53227
SB 950 # (not applicable)
Original date: 9/4/14
Revised: 2/17/15

DATA GAP STATUS

Chronic toxicity, rat:	No data gap, no adverse effect indicated*
Chronic toxicity, dog:	No data gap, no adverse effect indicated
Oncogenicity, rat:	No data gap, no adverse effect indicated*
Oncogenicity, mouse:	No data gap, no adverse effect
Reproduction, rat:	No data gap, no adverse effect indicated*
Developmental toxicity, rat:	No data gap, no adverse effect
Developmental toxicity, rabbit:	No data gap, no adverse effect
Gene mutation:	No data gap, no adverse effect
Chromosome effects:	No data gap, no adverse effect
DNA damage:	No data gap, no adverse effect
Neurotoxicity:	No data gap, possible adverse effect indicated.**

Cypermethrin (racemic mixture) is Chemical Code 2171, DPN 418

Zeta-Cypermethrin (enriched in S-isomers) has Chemical Code 5921, DPN 51970. S-Cypermethrin (a synonym for zeta-cypermethrin) has a unique Chemical Code (3866), but retains the same DPN No. (51970). There are very few records associated with that code.

* Data on cypermethrin was used to fill the data requirement.

** Data on zeta-cypermethrin was used to fill the rat subchronic neurotoxicity and developmental neurotoxicity data requirements.

Toxicology one-liners are attached.

All record numbers for the above study types through 282456 (Document No. 51970-0187) and 281290 (Document No. 53227-0013) were examined. This includes all relevant studies indexed by DPR as of 2/17/15.
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: T150217
Original by Aldous and Moore, Sept. 4, 2014, revised, Moore, 2/17/15.

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.

Table of Contents

METABOLISM AND PHARMACOKINETICS ** 3
GUIDELINE ACUTE STUDIES ON ACTIVE INGREDIENT 5
Acute oral toxicity, rat ** (Tox Category III) 5
Acute dermal toxicity ** (Tox Category III) 5
Acute inhalation toxicity, rat ** (Tox Category IV) 5
Primary eye irritation, rabbit ** (Tox Category III) 6
Primary dermal irritation ** (Tox Category III) 6
Dermal sensitization ** (not a sensitizer) 6
SUBCHRONIC STUDIES 7
Oral toxicity, rat: ** 7
Oral toxicity, non-rodent: ** † (Flagged for clinical signs typical of this chemical class) 7
Dermal toxicity, 21/28-day or 90-day: ** 8
CHRONIC STUDIES 8
Combined, rat ** (Bridge to Cypermethrin studies under DPN 418) 8
Chronic, dog 8
Oncogenicity, rat (See Combined Rat, above) 9
Oncogenicity, mouse ** 9
GENOTOXICITY 10
Bacterial reverse mutation assay ** 10

Mutagenicity: *In vitro* mammalian cell assay ** 10
Mutagenicity: *In vivo* cytogenetics ** 11
REPRODUCTIVE TOXICITY, RAT ** † (Bridge to Cypermethrin study: below) 12
DEVELOPMENTAL TOXICITY 12
Rat ** 12
Rabbit ** 13
NEUROTOXICITY 13
Acute neurotoxicity, rat ** † 13
90-day neurotoxicity, rat ** † [Bridge to zeta-cypermethrin study: 51970-0041 173639] 14
Developmental neurotoxicity, rat [A completed study is sought for bridging.] 14
Delayed neurotoxicity, hen (Not required at this time.) 15
IMMUNOTOXICITY ** 15
ENDOCRINE DISRUPTOR STUDIES (Not required at this time.) 16
SUPPLEMENTAL STUDIES 16

METABOLISM AND PHARMACOKINETICS **

NOTE: Collectively, the following studies adequately characterize phase 1 and phase 2 kinetics, excretion, primary metabolites, and lack of apparent effect of pre-treatment. The human study, Record No. 277347, serves more to document a means of exposure assessment than an assessment of metabolic disposition in humans. Aldous, 7/17/14.

53227-0010 277345 Hutson, D. H., "WL 85871: Metabolism of a single oral dose in the rat," Shell Toxicology Laboratory (Tunstall), Sittingbourne, Kent, England, Aug. 4, 1982, Laboratory Study #: AL-440-007, MRID #: 47944080. Five Wistar rats/sex were dosed once with [^{14}C-benzyl] WL 85871. Urine and feces were collected daily until sacrifice after 4 days. Excreta were evaluated after 2-dimensional TLC for metabolite analysis. Several tissues were assessed for radiolabel, in addition to points of entry or contamination (cagewash, intestines, skin, and carcass). In either sex, about 50% of administered dose was found in urine and about 40% in feces. Roughly 80% of label was recovered in the first 24 hours. Tissue contents after 4 days revealed concentration in fat about 10x higher than any organ evaluated (brain was consistently the lowest concentration). Still, no organs (other than intestine) contained over 0.1% of administered dose (0.1% of administered dose in liver). The most abundant metabolite identified was 3-(4-hydroxyphenoxy)benzoic acid O-sulfate ester (average of 38% of administered dose), a product of ester hydrolysis, hydroxylation of the distal phenyl ring, and conjugation. Other significant urinary metabolites were 3-phenoxybenzoic acid (5% of dose), and unconjugated 3-(4-hydroxyphenoxy)benzoic acid (4% of dose). The dominant moiety in feces was parent WL 85871 (22% of administered dose, constituting 74% of recovered label from TLC analyses of fecal samples). Apparently highly polar residues in feces constituted about 3% of administered dose. Study provides useful data on metabolic fate and distribution. Aldous, 8/15/14.

53227-0010 277346 Logan, C. J., "WL 85871: Depletion from tissues of female rats after a single oral dose," Shell Toxicology Laboratory (Tunstall), Sittingbourne, Kent, England, 3/24/83, Laboratory Study # AL-440-008. MRID #: 47944081. Groups of 3 female Wistar rats were dosed with 2 mg/kg WL 85871 (alpha-cypermethrin), and sacrificed after 1, 3, 8, 14, 16, 18, 22, or 42 days to examine kinetics of disappearance from fat (peri-renal, per-ovarian, or subcutaneous), skin, liver, and kidneys. Day 1 radioactivity (µg/g tissue) was highest in peri-renal and per-ovarian fat: about 3-fold higher than in liver. Concentration in subcutaneous fat was consistently somewhat lower than peri-renal and per-ovarian fat. Liver and kidney kinetics were monophasic, with $T_{1/2}$ of about 2 days, decreasing to undetectable levels by day 16. Skin and all fat categories indicated bi-phasic clearance, with initial phase $T_{1/2}$ of about 2 days, followed by phase 2 clearance $T_{1/2}$ of 19 to 40 days. When residues in peri-renal and per-ovarian fat were partitioned between hexane and acetonitrile at different sacrifice times, the hexane fraction (less polar) increased from 28% to 48% of respective total radioactivities between days 3 and 22. This indicated that lipophilic metabolites of WL 85871are either concentrated or stored in fats. This specialized study provides useful data on metabolic fate and distribution. Aldous, 8/15/14.

53227-0011 277350 Climie, I. J. G., "Cypermethrin: the kinetics of cypermethrin in the blood of rats following a single oral dose," Shell Research Limited, Sittingbourne, Kent, England, 8/28/80. BASF Registration Document No. CY-440-032, MRID 47944083. Investigators used about 50:50 ratios of cis and trans isomers of either ^{14}C-benzyl or ^{14}C-cyclopropyl labeled cypermethrin at concentrations of about 2 and 200 mg/kg. Peak plasma concentrations were obtained in either sex at about 2-4 hrs after dosing at 2 mg/kg, and at about 12-24 hrs after 200 mg/kg. Typical symptoms in high dose rats, such as ataxia, tremor, wide rear gate, and salivation, normally peaked at 3-4 hours after dosing (before the highest plasma levels were obtained). Following low doses with ^{14}C-benzyl label, the percent of plasma radioactivity identified as parent cypermethrin rose over time from 3% at 3-4 hrs after dosing to 17% (M) or 9% (F) at 9 hrs after dosing. Following low doses with ^{14}C-cyclopropyl label, the percent of plasma radioactivity identified as parent cypermethrin did not rise over time, and mean plasma concentration of parent compound was much lower than with ^{14}C-benzyl label. This result was confusing, since there should be no difference between parent levels because of label placement. Investigators concluded that these disparities were due to inter-animal variation. Data were not examined in further detail by Medical Toxicology Branch, since this racemic mixture is not the entity for which registration is sought. Aldous, July 3, 2014.

53227-0010 277347 van Sittert, N. J. and C. V. Eadsforth, "Human oral dose-excretion study with Fastac," Shell Internationale Petroleum Maatschappij B.V., The Hague, NL, Nov. 1, 1985, Laboratory Study # AL-445-003. MRID #: 47944082. Six human volunteers received single oral doses (gel capsule) of either 0.25, 0.50, or 0.75 mg Fastac (99.8% purity). Urine was collected daily for 4 days. Samples were dried after addition of $NaHCO_3$, then refluxed in H_2SO_4 render both the acid metabolite of Fastac and its glucuronide as the methyl ester of the acid (cis cyclopropane carboxylic acid). Product was extracted into hexane from basic solution, and assayed by glc with electron capture detection. After 3 weeks, the same volunteers received designated doses daily and daily urine collection for 5 days, with urine collection continuing for the next 5 days. Single dose administration yielded an average of 43% of administered dose during the first 24 hrs after dosing, with 1-7% of administered dose on the subsequent days. An

average of 49% of administered dose was obtained as the cis cyclopropane carboxylic acid on any given day after daily repeat dosing. Residues remaining after the first 24 hrs following the final dose were comparable to single-dose samples. This study was undertaken to evaluate this assay as a measure of exposure. Results indicate a useful assay. Useful supplementary data. Aldous, 7/7/14.

GUIDELINE ACUTE STUDIES ON ACTIVE INGREDIENT

Acute oral toxicity, rat ** (Tox Category III)

53227-0004; 277325; "BAS 310 I (Alpha Cypermethrin)-Acute Oral Toxicity Study in Rats"; (A.O. Garner, E. Leibold; Experimental Toxicology and Ecology, BASF Aktiengesellschaft, 67056 Ludwigshafen/Rhein, Germany; Study ID No. 10A0562/041081; 5/20/05); Three female Wistar rats were dosed orally by gavage with 50, 300, and 2000 (twice) mg/kg of BAS 310-I (Alpha Cypermethrin) Technical (batch no. COD-000165; purity: 98.8%) (vehicle: 0.5% carboxymethylcellulose in doubly distilled water). No deaths resulted from the treatment. No treatment-related clinical signs were evident throughout the 2-week observation period. No treatment-related lesions were noted in the necropsy examination. LD50 (F) > 2000 mg/kg; Toxicity Category III; **Study acceptable.** (Moore, 6/10/14)

Acute dermal toxicity ** (Tox Category III)

53227-0004; 277326; "**:** BAS 310 I (Alpha Cypermethrin)-Acute Dermal Toxicity Study in Rats"; (A.O. Garner, E. Leibold; Experimental Toxicology and Ecology, BASF Aktiengesellschaft, 67056 Ludwigshafen/Rhein, Germany; Study ID No. 11A0562/041082; 5/20/05); The skin of five Wistar rats/sex was exposed to 2000 mg/kg of BAS 310-I (Alpha Cypermethrin) Technical (batch no. COD-000165; purity: 98.8%) for 24 hours under a semi-occlusive wrap. Test material was moistened with 0.5% carboxymethylcellulose in doubly distilled water. No deaths resulted from the treatment. No clinical signs of systemic toxicity nor signs of irritation at the site of application were evident. No treatment-related lesions were noted in the necropsy examination. LD50 (M/F) > 2000 mg/kg; Toxicity Category III; **Study acceptable.** (Moore, 6/10/14)

Acute inhalation toxicity, rat ** (Tox Category IV)

53227-0004; 277327; "BAS 310 I (Alpha Cypermethrin)-Acute Inhalation Toxicity Study in Wistar Rats-4-Hour Dust Exposure"; (A.O. Garner, E. Leibold; Experimental Toxicology and Ecology, BASF Aktiengesellschaft, 67056 Ludwigshafen/Rhein, Germany; Study ID No. 13I0562/047014; 8/8/05); Five Wistar rats/sex/group were exposed nose-only to 1.07 and 2.47 mg/l (gravimetric) of BAS 310-I (Alpha Cypermethrin) Technical (batch no. COD-000165; purity: 98.8%) for four hours. The test material was mixed with Aerosol R972 (2% (w/w)) in order to enhance the aerosolization. The MMAD (GSD) values were 2.7 (2.7) and 2.8 (2.8) µm, respectively. No deaths resulted from exposure to 1.07 mg/l. One male and four females died in the 2.47 mg/l exposure group. Clinical signs included increased respiratory rate, salivation, apathy, squatting posture, ataxia, tremors and piloerection. Clinical signs were noted up to 7 days post-exposure. Dark red discoloration of the lungs was noted for two of the female animals which died prematurely. Otherwise, no other lesions were evident in the necropsy examination. LC50 (M) 2.79 mg/l, (F) 2.29 mg/ml; Toxicity Category IV; **Study acceptable.** (Moore, 6/10/14)

Primary eye irritation, rabbit ** (Tox Category III)

53227-0004; 277328; "BAS 310 I (Alpha Cypermethrin)-Acute Eye Irritation in Rabbits"; (M. Remmele; Experimental Toxicology and Ecology, BASF Aktiengesellschaft, 67056 Ludwigshafen/Rhein, Germany; Study ID No. 11H0562/042239; 5/19/05); The eyes of three New Zealand White rabbits were treated by ocular instillation with 0.1 ml (38 mg)/eye of BAS 310-I (Alpha Cypermethrin) Technical (batch no. COD-000165; purity: 98.8%). No corneal opacity nor iritis were evident throughout the 72-hour observation period. Conjunctival redness, grades 2 (1/3) and 1 (2/3) was evident at 24 hours, diminishing to grade 1 (1/3) at 48 hours and clearing by 72 hours. Chemosis, grade 1 (1/3), was noted at 24 hours, clearing by 48 hours. No discharge was evident at 24 hours post-dose. Toxicity Category III; **Study acceptable.** (Moore, 6/11/14)

Primary dermal irritation ** (Tox Category III)

53227-0004; 277329; "BAS 310 I (Alpha Cypermethrin)-Acute Dermal Irritation in Rabbits"; (M. Remmele, E. Leibold; Experimental Toxicology and Ecology, BASF Aktiengesellschaft, 67056 Ludwigshafen/Rhein, Germany; Study ID No. 18H0562/042238; 5/19/05); The skin of 3 New Zealand White rabbits was exposed to 0.5 ml/site, one site/animal, of BAS 310-I (Alpha-Cypermethrin) Technical (batch no. COD-000165; purity: 98.8%) for 4 hours under a semi-occlusive wrap. The test material was moistened with distilled water. Erythema, grades 2 (2/3) and 1 (1/3), was noted at 1 and 24 hours post-dose, grade 2 (2/3) at 48 and grades 3 (1/3) and 2 (1/3) at 72 hours, grade 2 (1/3) at 7 days and clearing by day 14. Edema, grade 2 (1/3), was evident at 72 hours. Toxicity Category III; **Study acceptable.** (Moore, 6/11/14)

Dermal sensitization ** (not a sensitizer)

53227-0004; 277330; "BAS 310 I (Alpha Cypermethrin)-Maximization Test in Guinea Pigs"; (A.O. Garner, E. Leibold; Experimental Toxicology and Ecology, BASF Aktiengesellschaft, 67056 Ludwigshafen/Rhein, Germany; Study ID No. 30H0562/042240; 6/27/05); Ten female Hsd Poc: DH guinea pigs were treated initially in the induction phase by intradermal injection with two doses each of 0.1 ml of 5% preparation of BAS 310-I (Alpha- Cypermethrin) Technical (batch no. COD-000165; purity: 98.8%) in an aqueous 1% carboxymethyl cellulose (CMC) preparation, 0.1 ml of a 5% preparation of the test material in Freund's adjuvant: 0.9 aqueous NaCl solution (1:1), and 0.1 ml of Freund's adjuvant: 0.9 aqueous NaCl solution (1:1). One week later, the skin of each animal was exposed to 1 g/site of 50% preparation of the test material in an aqueous 1% CMC solution under an occlusive wrap for 48 hours. A group of five control animals was treated in the same manner except that they were exposed only to the vehicle. Fourteen days after the dermal application, the skin of each animal in the treated and control groups was exposed to 0.5 g/site of a 50% preparation of the test material in an aqueous1% CMC solution for 24 hours under an occlusive wrap. In the challenge, no signs of dermal irritation were evident for either the treated or the control groups at 24 or 48 hours post-exposure. The test material is not a contact dermal sensitizer in accordance with the Guinea Pig Maximization Test. The positive control was functional. **Study acceptable.** (Moore, 6/11/14)

SUBCHRONIC STUDIES

Oral toxicity, rat: **

53227-0006 277332 Clark, D. G., "WL 85871: A 90 day feeding study in rats," Shell Toxicology Laboratory (Tunstall), Sittingbourne, Kent, England, 7/30/82. Laboratory Study #AL-425-003. MRID # 47944068. The main (13-wk) study involved 40 control rats/sex plus 20/sex in treatment groups of 20, 60, 180, or 540 ppm of WL 85871 (alpha-cypermethrin), Batch OCD/7 (96.5% pure with respect to the two isomers that are enriched in the technical). Investigators did not compute mg/kg/day dose received. Additional groups, primarily for 6-week hematology and clinical chemistry, were one-half of the above group sizes at the same dose levels. Parameters evaluated in the main (13-wk) study, typical of studies in this time period, included clinical signs, body weight, food consumption, hematology, clinical chemistry, urinalysis, terminal necropsy with organ weights, and histopathology. Subchronic NOEL = 60 ppm, based on modestly (statistically significantly) elevated relative liver weights at 180-540 ppm in both sexes. Common findings at 540 ppm in both sexes included markedly reduced food consumption (especially in the first 1-2 weeks) and substantial body weight decrements through the study. Abnormal gait (with splayed hindlimbs), seen only in three 540 ppm males, was likely due to treatment. Slight increases in skin sore(s) and/or fur loss in 540 ppm males were plausibly treatment-related. Urine tended to be marginally more acidic in 540 ppm males, and urine volume was slightly reduced and specific gravity slightly elevated in high dose males and females at both time points: there were no associated indicators of kidney pathology. Treatment did not elicit any histopathology. Study is acceptable, with several deficiencies with respect to current standards. There **were no adverse effects. Aldous, 6/25/14.

Oral toxicity, non-rodent

****53227-0007 277333** Greenough, R. J., J. B. Cockrill, and R. Goburdhun, "WL 85871: A 13-week oral (dietary) study in dogs," Inveresk Research International, Musselburgh, Scotland, Nov. 1, 1984. Laboratory Study # AL-425-005. MRID #: 47944069. Beagles were dosed with WL 85871 (Alpha-cypermethrin Technical), Batch F830047B, purity 95.8%, for 13 weeks in a basic subchronic study design. There were 4, 4, 4, or 6 dogs/sex at dose levels of 0, 30, 90, and 270 ppm, respectively. Nominal achieved dose levels were about 1.2, 3.4, and 10.7 mg/kg/day for treated males, and 1.3, 3.8, and 11.2 mg/kg/day for females. **NOEL for males and females = 3.4 and 3.8 mg/kg/day** respectively, based on clinical signs of neurotoxicity. Signs consistent with this class of pesticide were evident in all high dose males and females, such as whole body tremors, head nodding, lip licking, ataxia, and (beginning at week 3) a characteristic high-stepping gate. Subdued behavior was seen occasionally. Some signs, such as the tremors, were seen more frequently as the study progressed. Duration of clinical signs became progressively longer as the study progressed: signs initially observed for the first 3-6 hours after dosing were commonly observed to carry over to the following day prior to dosing in later study weeks. One 270 ppm female showing these signs was humanely sacrificed during week 5, evidently due to treatment. **Study is acceptable**, with deficiencies noted in DPR review. **Clinical signs, expected with this class of pesticides, are designated as "possible adverse effects**." Aldous, 6/27/14.

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

418-0324 277763 Henderson, C. and G. R. Parkinson, "Cypermethrin Technical: Subacute Dermal Toxicity Study in Rabbits," ICI Central Toxicology Laboratory, Alderley Park, Macclesfield, UK, Feb. 4, 1981. Laboratory Study # CTL/P/588. Ten NZW rabbits/sex/group were dosed dermally 5 days/wk, 6 hrs/day, for 3 weeks (15 exposures/animal) at 0, 2, 20, or 200 mg/kg per treatment day. Of any 10/sex/group, 5 had abraded skin (sufficient to penetrate the stratum corneum, but not to cause bleeding), and the other 5 had intact skin. After the removal of dressings and gentle washing on treatment days, rabbits were wrapped in a tubular stockinette, which prevented ingestion of residual test article, and may have limited any effects of scratching due to expected paresthesia (likely contributing to skin irritation, below). Subacute systemic **NOEL = 200 mg/kg per treatment day (no subacute effects). Application site skin irritation was observed or was increased in incidence or degree at 20 to 200 mg/kg per treatment day in both sexes. Common signs were erythema, edema, thickening, desquamation, flaking, cracking, and occasional wrinkling or necrosis. Irritation was particularly evident in females. Acute clinical signs evaluation was not a primary study objective, such that clinical sign evaluations were only recorded just prior to treatment (i.e. when transitory responses from the previous dosing had generally subsided). **Study is acceptable**, with several noted deficiencies. No adverse effects were indicated. Aldous, 7/16/14.

CHRONIC STUDIES

Combined, rat

418-041; 037987; "Cypermethrin: 2 Year Feeding Study in Rats", Report No: CTL/P/669; G.M. Milburn, D. Forbes, P.B. Banham, I.S. Chart, M.J. Godley, C.W. Gore, I. Pratt, M.D.C. Scales, M.D. Stonard, and B.H. Woollen; Imperial Chemical Industries PLC, UK; 6/28/82. Groups of 64 or 128 (0 ppm) Wistar rats/sex were given cypermethrin (batches P19, P24, P26; 88.2 to 93.1% stated purities) in the diet at 0, 20, 150, or 1500 ppm for 104 weeks. At 52 weeks 12 or 24 (0 ppm) rats/sex/group were sacrificed. The high dose was initially 1000 ppm but was raised to 1500 ppm between weeks 3 and 6. Effects seen in both sexes at 1500 ppm were: decreased incidence of distended abdomen, body weight gain, food consumption, red cell volume, plasma cholesterol, plasma triglycerides, urine volumes, and liver, kidney, spleen and heart weights; and increased incidence of hair loss, lymphocyte count, plasma urea, and liver aminopyrine N-demethylase activity and smooth endoplasmic reticulum **(NOEL = 150 ppm). **No adverse effect was indicated**. The **study was unacceptable (J. Christopher, 8/27/85; S. Morris and J. Gee, 3/17/94) but upgraded by evaluation of the collective data** (H. Greene and S. Morris, 1/12/1).

Chronic, dog

** 53227-0007, 0013; 277334, 281290; Dean, I. and F. Jackson "WL 85871: 52-week oral (dietary) toxicity study in dogs," Inveresk Research International, Tranent, Scotland, 4/18/95. MRID #: 47944070. BASF Registration Document No. AL-427-001. Four beagles/group were dosed in diet with WL85871 (alpha-cypermethrin), Batch ST91/243, at 0, 60, 120, or 240 ppm ((M) 0, 2.03, 4.17, 8.08 mg/kg/day, (F) 0, 2.19, 4.28, 8.68 mg/kg/day, calculated by reviewer). NOEL = 60 ppm, due to apparent paresthesia, evidently leading to scratching and eventual inflammation or ulceration of tails in two 240 ppm males, abdominal hair loss on an additional 240 ppm male, and hair loss on hind limbs and abdominal skin of one 120 ppm female. There were transient minor initial food consumption decrements in both sexes during the first 2 weeks

of the study at 240 ppm. Prostate weights in 240 ppm males appeared to be meaningfully reduced compared to controls. There was no associated histopathology. Previously, the study was deemed to be unacceptable for the following reasons. Purity, primary isomer characterization, and stability data of Batch ST91/243 were not provided. Validation of the stability of dietary formulations was not presented in the report. In addition, the present study found no evidence of tremors or other characteristic signs of pyrethroid toxicity (except for indications of paresthesia which led to scratching and infections). The subchronic study with alpha-cypermethrin performed about 10 years earlier at a similar highest dose level found most dogs showing significant neurotoxicity effects which became more persistent over the course of the study. The registrant has submitted sufficient information to document the purity of the test material and the homogeneity and stability of the test material in the dietary preparations (see record no. 281290, exhibit 3). The absolute and relative prostate weights of the 270 ppm rats in the rat subchronic dietary toxicity study were 78% of the males in the control group. By the termination of this study, the mean absolute and relative prostate weights of the 240 ppm males were 64.5 and 63.5%, respectively of the control group. Although no target of toxicity was apparent for the prostate gland, the prostate seemed to be affected by the treatment. For the apparent inconsistency in the manifestation of clinical signs, the males and females in the subchronic study consumed 10.7 and 11.2 mg/kg/day, respectively, of the active ingredient. The males and females in the chronic toxicity study consumed 9.1 and 9.3 mg/kg/day, respectively, during the initial 13 weeks of the study. The possibility remains that a treatment level of 10 mg/kg/day or above represents a threshold level for the manifestation of the more serious neurotoxicity effects. **No adverse effect indicated. Rat Chronic Dietary Toxicity NOEL:** 60 ppm ((M) 2.03 mg/kg/day, (F) 2.19 mg/kg/day) (based upon the incidence of apparent paresthesia suffered by one animal in the 120 ppm treatment group). **Study acceptable.** (Aldous, 8/13/14, upgraded, Moore, 12/24/14)

Oncogenicity, rat

See combined rat above.

Oncogenicity, mouse

53227-0008 277335 Green, C. F., "Alphacypermethrin: oncogenicity study by dietary administration to CD-1 mice," Huntingdon Life Sciences Ltd, Eye, Suffolk, England, 5/20/99 (amended). BASF Registration Document No. 1999/7002664. MRID # 47944071. Groups of 52 CD-1 mice/sex/group were dosed in diet with Alpha-cypermethrin (95.4% purity, Batch 02156) for 78 weeks in an oncogenicity study. Mice received 0, 30, 100, or 300 ppm of the technical, equivalent to 3.0, 10.6, or 35 mg/kg/day in treated males and 3.5, 11.5, or 38 mg/kg/day in females. An additional 20 mice/sex/group were allocated to a 1-year chronic study. **NOEL = 30 ppm (3.0 mg/kg/day) in males, based on body weight decrements and signs likely relating to paresthesias commonly observed in this class of chemicals, such as ungroomed appearance and hair loss. Females had body weight decrements at 300 ppm only, with NOEL = 100 ppm or 11.5 mg/kg/day. Increased frequencies of piloerection and of encrustations of dorsal and ventral surfaces were observed in 300 ppm males. **Study is acceptable, with no adverse effects.** Aldous, 6/13/14.

GENOTOXICITY

Bacterial reverse mutation assay

** 53227-0009; 277340; "Fastac TM: Bacterial Mutagenicity Studies"; (T.M. Brooks, D.E. Wiggins; Sittingbourne Research Centre, Sittingbourne, Kent, ME9 8AG, England; Study ID No. SBTR.92.022; 2/16/93); *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538 and *Escherichia coli* strain WP2 *uvrA* were exposed to concentrations of Fastac Technical (Alpha-Cypermethrin Technical) (batch no. 02156; purity: 95.6%) ranging from 31.25 to 5000 µg/plate under conditions of non-activation and activation. The cells were exposed to the test material for 48 to 72 hours at 37° C, using the plate incorporation procedure. Each treatment level was performed in the triplicate with two trials. An Aroclor 1254-induced rat liver S9 fraction was used to metabolize the test material. **No adverse effect indicated.** There was no increase in the incidence of revertant colonies under conditions of either activation or non-activation. Positive controls were functional. **Study acceptable.** (Moore, 6/26/14)

53227-0009; 277339-842; "Genotoxicity Studies with Fastac – The Induction of Gene Mutation in the Yeast *Saccharomyces cerevisiae* XV185-14C"; (T.M. Brooks; Sittingbourne Research Centre, Biotechnology and Toxicology Directorate, Sittingbourne, Kent, ME9 8AG, England; Study ID No. SBGR.84.117; 4/18/84). *Saccharomyces cerevisiae* XV185-14C cells were exposed to concentrations of Fastac Technical (alpha-cypermethrin technical) (batch nos. F830047B, RS0016/84; purity: 95.8% (cis 1: cis 2 isomer ratio: 3.0/97.0)) ranging from 31.25 to 4000 µg/ml with and w/o activation. One trial was performed on cells in the log phase of growth and the other was performed on cells in the stationary growth phase. Both reverse and forward mutation assays were performed. In the reverse mutation assay, revertants to markers arg 4-17, trp 5-48 and hom 3-10 were enumerated. In the forward assay, cycloheximide-resistant colonies were selected. There was no treatment-related increase in the number of mutant colonies under conditions of non- activation in either trial. Under conditions of activation, there was no increase in the number of mutant colonies as well. However, treatment with the positive control, cyclophosphamide, did not result in a positive response. In the forward mutation assay with cells in the log phase of growth, there was no treatment-related increase in the mutation numbers under conditions of non-activation and the positive control was functional. In the activation assay, there was no evidence of a treatment-related effect on the number of cell mutations. However, the positive control was not functional. For the forward mutation assay in the stationary phase, no study results were forthcoming (no growth on the plates). **No adverse effect was evident. Study supplemental** (study is not one which is set forth in the OPPTS guideline protocols; the positive control for activation was not functional; the forward mutation assay with cells in the stationary phase did not result in usable data). (Moore, 6/25/14)

Mutagenicity: *In vitro* mammalian cell assay

** 53227-0009; 277342; "Evaluation of the Mutagenic Activity of Fastac Technical in an *In Vitro* Mammalian Cell Gene Mutation Test with L5178Y Mouse Lymphoma Cells (with Independent Repeat)"; (E.J. van de Waart; NOTOX B.V., 5231 DD's-Hertogenbosch, The Netherlands; Study ID No. NOTOX 087367; Mouse lymphoma L5178Y cells (clone 3.7.2C ($TK^{+/-}$)) were treated with Fastac Technical (Alpha-Cypermethrin Technical) (batch no. ST91/243; purity: 95.4%) at concentrations ranging from 1.0 to 50 µg/ml (+/- activation) for 2 hours at 37°C in both trials. Single cultures were performed for each treatment level. An Aroclor 1254-induced rat liver S9 fraction was used to metabolize the test material. There was

no treatment-related increase in the mutation frequency under conditions of either activation or non-activation. The positive controls were functional. **No adverse effect indicated. Study acceptable.** (Moore, 7/1/14)

Mutagenicity: *In vivo* cytogenetics

** 53227-0009; 277341; "Fastac TM: *In Vitro* Chromosome Studies Using Cultured Human Lymphocytes"; (T.M. Brooks, D.E. Wiggins; Sittingbourne Research Centre, Sittingbourne, Kent, ME9 8AG, England; Study ID No. SBTR.93.007; 4/27/93); Primary human lymphocyte cultures, procured from the whole blood of volunteers (stimulated with PHA for 48 hours), were treated with concentrations of Fastac Technical (Alpha-Cypermethrin Technical) (batch no. 02156; purity: 95.6%) ranging from 3.91 to 1000 µg/ml for 24 and 48 hours with and w/o activation. In a second experiment, in the assay with activation, cells were exposed to the same concentrations of the test material for 3 hours, followed by an additional 21 hours of incubation. For the non-activated assay, the cells were exposed to concentrations ranging from at least 93.75 to 750 µg/ml for 24 hours. There were duplicate samples per treatment level. An Aroclor 1254-induced rat liver S9 fraction was used to metabolize the test material. No treatment-related increase in chromosomal aberrations was evident in the assay. The positive controls were functional. **No adverse effect indicated. Study acceptable.** (Moore, 6/27/14)

** 53227-0009; 277343; "Genotoxicity Studies with Fastac: *In Vivo* Cytogenetic Test Using Rat Bone Marrow"; (M.G. Clare, D.E. Wiggins; Sittingbourne Research Centre, Sittingbourne, Kent, ME9 8AG, England; Study ID No. SBGR.84.120; 5/9/84); Six Wistar rats/sex/group were dosed orally by gavage with 0 (vehicle: corn oil), 2, 4, or 8 mg/kg of Fastac Technical (Alpha-Cypermethrin Technical) (batch nos. F830047B, RS0016/84; purity: 95.6%). A positive control cohort of 7 animals/sex/group were dosed with 25 mg/kg of cyclophosphamide by intraperitoneal injection or with 40 mg/kg of cyclophosphamide orally by gavage. At 24 hours post-dose, the animals were euthanized. Two hours prior to sacrifice, each animal was injected ip with colchicine (4 mg/kg). At sacrifice, both femurs were procured and the bone marrow was recovered and processed for analysis. The mitotic index was determined for each animal and up to 200 cells at metaphase were analyzed for the presence of structural chromosomal aberrations and polyploidy. There was no treatment-related increase in structural chromosomal aberrations or incidence of polyploidy. **No adverse effect indicated.** The positive control was functional. **Study acceptable.** (Moore, 7/2/14)

** 53227-0009; 277344-844; "Micronucleus Test in Bone Marrow of the Mouse with Fastac Technical"; (E.J. van de Waart; NOTOX B.V., 5231 DD's-Hertogenbosch, The Netherlands; Study ID No. NOTOX 087378; 1/17/95); Fifteen Swiss OF-1 mice/sex/group were dosed orally by gavage with 0 (vehicle: corn oil), 1, 5, or 10 mg/kg of Fastac Technical (Alpha-Cypermethrin Technical) (batch no. ST91/243; purity: 95.4%). Five animals/sex/group/time point were euthanized at 24, 48 or 72 hours post-dose. A positive control group of 5 animals/sex were dosed orally by gavage with 50 mg/kg of cyclophosphamide and euthanized at 48 hours post-dose. One thousand polychromatic erythrocytes (PCE)/animal were examined for the presence of a micronucleus. In addition, the ratio of polychromatic to normochromatic erythrocytes (NCE) was determined. There was no treatment-related increase in the number of micronucleated PCE per 1000 PCE. **No adverse effect indicated.** The positive control was functional. **Study acceptable.** (Moore, 7/2/14)

REPRODUCTIVE TOXICITY, RAT

****418-045; 037991**; "Cypermethrin: Three Generation Reproduction Study in the Rat", Report No: CTL/P/683; G.M. Milburn, P.B. Banham, R.D.N. Birtley, M.J. Godley, and S.F. Moreland; ICI Central Toxicology Laboratory, Alderley Park, UK; 7/9/82. Groups of 15 male and 30 female Wistar rats were continuously exposed to diets containing cypermethrin (batches P19, P24, P26; 91.5, 93.1, 90.6% stated purity) at 0, 50, 150, or 750 ppm for 3 generations (F0, F1, F2) with 2 litters/generation (F1a, F1b, F2a, F2b, F3a, F3b). The high dose F0's received 1000 ppm for the first 12 weeks and 750 ppm thereafter. The F0's were first bred at 12 weeks. Ten days after weaning the F1a pups the F0's were bred again to produce the F1b pups. Selected F1b weanlings were exposed for 11 weeks then bred similarly to the F0's to produce the F2a and F2b litters. This cycle was repeated with selected F2b weanlings to produce the F3a and F3b litters. The initial high dose of 1000 ppm produced transient neurological effects between days 3 and 22 in the majority of both sexes of the F0 parents and the death of one male on day 9. Decreased adult body weight gain was seen in F0's in both sexes at 1000 ppm and females at 150 ppm; in F1 females at 750 ppm; and both F2 sexes at 150 and 750 ppm. Adult food consumption was reduced for both F0 sexes at 1000 ppm and F0 females at 150 ppm; and both F1 and F2 sexes at 750 ppm **(parental NOEL = 50 ppm).** There were no treatment-related effects on reproductive parameters. A possible adverse effect was indicated by group mean pup weight gains in the 750 ppm group that were less than controls: for both sexes in all litters at 21, and 28 days post-partum and for both sexes in the F1A, F1B, F2B, and F3B litters at 10 days post-partum and in pilot studies decreased live litter size and pup survival at 750 and 1000 ppm and, decreased birth weights and body weight gain at 1000 ppm and in weaned pups, increased incidences of ataxia, gait abnormalities and hypersensitivity to noise and decreased pup body weight in both sexes at **1000 ppm (developmental NOEL = 150 ppm). The study was unacceptable (S. Morris and J. Gee, 3/1/94) but upgraded by with adequate submissions of analytical data for the test material, a rationale for the high dose, compiled gross and histopathology observations, compiled male reproductive and mating performance data, and individual and compiled clinical data for all animals for the entire study** (S. Morris and J. Gee, 6/21/1).

DEVELOPMENTAL TOXICITY

Rat

** 53227-0009; 277337; “Alphacypermethrin: Oral (Gavage) Rat Developmental Toxicity (Teratogenicity) Study”; (L.F.H. Irvine; Toxicology Laboratories Limited, Ledbury, Herefordshire HR8 1LH, England; Study I.D. No. SLN/2/R; 3/7/94); Twenty four- mated Sprague-Dawley female rats/group were dosed orally by gavage with 0 (vehicle: corn oil), 3, 9, and 18 mg/kg/day from gestation day 6 through 15. Due to the severity of clinical signs for the 18 mg/kg treatment group, the treatment level was adjusted to 15 mg/kg/day on gestation day 10. An additional group of 24 mated females was treated with 15 mg/kg/day of the test material from gestation day 6 through 15. The mean body weight gain and food consumption of the dams in the 15 mg/kg and 18/15 mg/kg treatment groups were less than the control values ($p<0.01$ or 0.001). The mean body weight of the fetuses in the 15 mg/kg treatment group was less than that of the control group ($p<0.05$). Otherwise, there was no other effect on fetal development. **No adverse effect evident. Maternal NOEL:** 9 mg/kg/day (based upon the treatment-related effect on mean body weight gain and food consumption of the 15 mg/kg treatment group); **Developmental**

NOEL: 9 mg/kg/day (based upon the treatment-related effect on the mean fetal weights of the 15 mg/kg treatment group); **Study acceptable.** (Moore, 6/24/14)

Rabbit

** 53227-0009; 277336; "Alphacypermethrin: Oral (Gavage) Rabbit Developmental Toxicity (Teratogenicity) Study"; (L. F.H. Irvine; Toxicology Laboratories Limited, Ledbury, Herefordshire HR8 1LH, England; Study ID No. SLN/4/93; 3/7/94); Sixteen time-mated female New Zealand White rabbits/group were dosed orally by gavage with 0 (corn oil), 3, 15 or 30 mg/kg/day of Alphacypermethrin (WL 085871) (batch no. ST 91/243; purity: 95.6%) from day 7 through day 19 of gestation. Four does had to be removed from the study prior to the initiation of the dosing due to low weight gain and food consumption. Two does in the control group, 3 does in the 15 mg/kg group and two does in the 30 mg/kg group were euthanized *in extremis* between days 15 and 22 of gestation due to severe weight loss. There was no apparent treatment-related effect upon the mean body weight gain or food consumption of the surviving animals. There was no treatment-related effect on fetal survival or development. **No adverse effect indicated. Maternal NOEL:** 30 mg/kg/day (based upon the lack of a treatment-related effect on the 30 mg/kg treatment group); **Developmental NOEL:** 30 mg/kg/day (based upon the lack of a treatment-related effect upon the fetuses in the 30 mg/kg treatment group); **Study acceptable.** (Moore, 6/23/14)

NEUROTOXICITY

Acute neurotoxicity, rat

53227-0005; 277331; "WL85871 (Fastac): An Acute Oral (Gavage) Neurotoxicity Study in the Rat"; (G.N. Fokkema; Sittingbourne Research Centre, Sittingbourne, Kent ME9 8AG, England; Study No. SBTR.92.027; 12/20/93); Ten Crl:CD:BR rats/sex/group were dosed orally by gavage with 0 (vehicle: corn oil), 4, 20 or 40 mg/kg of WL85871 (Fastac) (Alpha-Cypermethrin Technical) (batch no. 02156; purity: 95.6%). Due to inadequate whole body perfusion at the termination of the study, a second study was performed for the purpose of correcting this error in which 5 animals/sex/group were dosed with 0, 4, 20 or 40 mg/kg of the test material (an additional 1 male in both the 20 and 40 mg/kg groups were added due to deaths in these groups). The mean body weight of the males at 7 days post-dose was less than that of the control group. Clinical signs for the 20 and 40 mg/kg treatment groups included prostration, thrashing, writhing, abnormal gait, splayed gait, piloerection, and increased salivation. The signs were more prevalent in the males. In the Functional Observational Battery (FOB) at 5 hours post-dose, the males in the 20 and 40 mg/kg groups were more hyperactive in the cage, were more difficult to remove from the cage and handle, were more unkempt in appearance, and demonstrated greater variability in degree of arousal and an abnormal gait. Their fore- and hindlimb extension was abnormal and their righting reflex was affected. The females were affected to a lesser degree. The fore- and hind-limb grip strength of the 4 mg/kg group and above was less than that of the control group at 5 hours post-dose. The grip strength of the females was not affected. In the motor activity assessment, the males in the 40 mg/kg group demonstrated both a total increased time of movement and an increased number of movements at 5 hours post-dose. The 40 mg/kg females had a reduction in time of movement and in the number of movements at the 5 hour post-dose time point. In the histopathology, an increased incidence of fiber degeneration was noted in the proximal and distal sciatic nerves of both sexes in the 20 and 40 mg/kg treatment groups. **Possible adverse effect:** neurotoxicity noted in the

clinical signs and FOB observations and histopathology. **Rat Acute Oral Neurotoxicity NOEL:** (M/F): 4 mg/kg (based upon the incidence of clinical signs, FOB observations and/or histopathology noted for both sexes in the 20 mg/kg treatment group); **Study acceptable.** (Moore, 6/19/14)

90-day neurotoxicity, rat

****51970-0041 173639** Freeman, C., "Zetacypermethrin Technical subchronic neurotoxicity screen in rats," FMC Corporation, Princeton, NJ, 9/22/99. Study No. A98-4874. MRID # 44962202. Groups of 10 Long Evans rats were dosed in diet with Zeta-cypermethrin for 13 weeks at 0, 75, 400, or 750 ppm. This technical was 95.3% to 96.7% total cypermethrin, of which 85.0% to 87.0% comprised zeta isomers. Estimated achieved doses were 5.0, 26, and 47 mg/kg/day in treated males, and 5.9, 32, and 56 mg/kg/day in females. All rats were subject to routine evaluations such as clinical signs, plus FOB, and motor activity evaluations pre-test and at weeks 4, 8, and 13. Five/sex of controls and 750 ppm group received a thorough neurohistopathology examination after *in-situ* perfusion. **NOEL for subchronic responses for males was 75 ppm (5.0 mg/kg/day)** due to dose-related reduction in food consumption and body weights, as well as decreased motor activity counts (with normal accommodation). **Subchronic NOEL for females = 400 ppm (32 mg/kg/day), based on diminished body weight and food consumption.** Diminished food consumption and body weight for the first study week in 400 ppm females is probably treatment-related, but is best considered an acute response. There was no neurohistopathology change**. Study is acceptable, with decreased motor activity as a "possible adverse effect.**" Aldous, Sept. 4, 2014.

Developmental neurotoxicity, rat

53227-0009 277338 Chukwedebe, A., "Substantial similarities and concordances in the developmental neurotoxicity potentials of alpha-cypermethrin and zeta-cypermethrin," 07/02/2009, BASF Corp. This is an argument justifying bridging between the different isomeric forms of cypermethrin, and provides comparisons of many toxicological parameters between cypermethrin, alpha-cypermethrin, and zeta-cypermethrin. In particular, pp. 6-7 of this analysis argue that a developmental neurotoxicity (DNT) study on zeta-cypermethrin (not on file with DPR) found no DNT adverse effects, and recommended that the zeta-cypermethrin DNT study results could be applied to the other isomer variants of cypermethrin. DPR reviewer (Aldous) recommends that the zeta-cypermethrin DNT study be obtained for review. There is no DPR "review" for this record, which is itself a review. Aldous, 8/29/14.

** 51970-0187; 282456; **"**A Dietary Developmental Neurotoxicity Study of Zeta-Cypermethrin Technical in Rats"; (M.D. Nemec; WIL Research Laboratories, LLC, Ashland, OH; Study No. A2004-5809; 8/24/05); Twenty five-mated female Sprague Dawley rats/group received 0, 50, 125 or 300 ppm of Zeta-Cypermethrin Technical (lot no. PL03-0427; purity: 81.8%) in the diet from gestation day 6 through lactation day 21 (a.i. uptake: gestation, 0, 3.6, 9.0, 21.1 mg/kg/day, lactation: 0, 8.7, 21.4, 48.7 mg/kg/day). Offspring from 23, 25, 22, and 25 litters in the control and three treated groups, respectively, were assessed neurologically for up to 70 days post-natal in a functional observational battery, motor activity assessment, auditory startle response, and Biel Maze learning and memory assessments. The neuropathologic examination and morphometric analysis of the brain and other selected neurological tissues from the F1 generation were performed. No treatment-related maternal mortalities occurred during the treatment period. For the F1 generation, no deaths occurred post-weaning among the study

animals. The mean body weights and food consumption of the 300 ppm dams were less than the control group values throughout the lactation period ($p < 0.01$ or 0.05). The mean body weights of the 300 ppm pups and young adult animals of both sexes were less than those of the control group throughout much of the study period (NS). There was no treatment-related effect on the live birth, viability or lactation indices. For the developmental landmarks, the preputial separation for the male pups and the time to vaginal opening for the female pups, were not affected by the treatment. In the detailed observational battery, no treatment-related effects were noted for the dams. For the F1 generation, in the Functional Observational Battery, the fore limb grip strength of the 300 ppm males was less than that of the control group on post-natal day 22 ($p<0.05$). However, the lower mean body weights of the animals in this group likely affected their grip strength. No other statistically significant effect was noted for this parameter at post-natal day 45 or 60. The 300 ppm females at post-natal day 20 demonstrated an increased latency to VMax (TMax) ($p<0.05$). The 300 ppm males also demonstrated this increased latency at 60 days post-natal (NS). The effect did not appear to be of physiological significance. There was no apparent treatment-related effect noted in the Biel Maze test for either of the two time points which were evaluated. In the necropsy examination, there was no treatment-related effect upon the brain weight for either 21 or 72 day old animals. In the neurohistopathological examination and brain morphometry, no treatment-related lesions were evident in the brains of the F1 generation examined on post-natal days 21 or 72 or in the other nervous tissues at post-natal day 72. **No adverse effect indicated. Maternal NOEL:** 125 ppm (9.0 mg/kg/day) (based upon the lower mean body weights of the 300 ppm dams); **Developmental Neurotoxicity NOEL:** 300 ppm (48.7 mg/kg/day) (based upon the lack of neurotoxic effects on the F1 generation offspring in the 300 ppm group); **Study acceptable.** (Moore, 1/30/15)

Delayed neurotoxicity, hen

Not required at this time.

IMMUNOTOXICITY

53227-0010 277349 Buesen, R., V. Strauss, S. Groeters, E. Fabian, and B. van Ravenzwaay, "BAS 310 I (Alphacypermethrin) – immunotoxicity study in male Wistar rats – administration via the diet for 4 weeks, " BASF, Ludwigshafen/Rhein, Germany, 10/20/2010, BASF Registration Document No. 2010/1057357. MRID #: 48273201. Eight male rats/group were administered 0, 50, 150, or 450 ppm BAS 310 I (Alphacypermethrin), 99.2% purity, Batch COD-000595 for 4 weeks in a guideline immunotoxicity study, with key endpoints of sheep red blood cell (SRBC) response, and organ weights of spleen and thymus. Achieved levels in treated rats were 4, 12, and 34 mg/kg/day. Positive control was cyclophosphamide monohydrate (4.5 mg/kg/day for 4 weeks). Alpha-cypermethrin rats were clinically normal, with body weight and food consumption unaffected, and with no effect on SRBC response, or on spleen and thymus organ weights, or on gross necropsy. Cyclophosphamide rats showed only about 20% of untreated group SRBC response, and spleen and thymus weights were highly significantly reduced, as expected. **Study is acceptable, with no adverse effects. Aldous, July 9, 2014.

53227-0010 277348 Buesen, R., "Summary report: BAS 310 I – Test study in Wistar rats – Administration in the diet for 2 weeks," BASF, Ludwigshafen/Rhein, Germany, Feb. 10, 2010, BASF Registration Document No. 2010/1017329. MRID No. 48273202. This was a range-finding study for a subsequent immunotoxicity study (DPR Record No. 277349). In this non-

GLP study, 3 Wistar rats/sex/group were dosed for 2 weeks with alpha-cypermethrin at 0, 50, 150, or 450 ppm. Reported achieved dose levels in treated rats were 4.7, 14, and 40 mg/kg/day in males, and 4.7, 13, or 39 mg/kg/day in females. There were no clinical signs or premature deaths. Food consumption was reduced by about 20% in both sexes during days 0-3 at 450 ppm, and by lesser amounts at later intervals. Body weight gains were reduced at 450 ppm in both sexes, particularly also during days 0-3. Responses indicated that these dose levels would be suitable for the cited immunotoxicity study. Aldous, July 8, 2014.

ENDOCRINE DISRUPTOR STUDIES

Not required at this time.

SUPPLEMENTAL STUDIES

See under Developmental Neurotoxicity, above, for comparative toxicity of cypermethrin, alpha-cypermethrin, and zeta-cypermethrin across several study types. This analysis may be of interest in the event of comparative risk assessment.