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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

005549
OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

OCT 21 1986

MEMORANDUM

SUBJECT: EPA ID No. 4822-EOU; Toxicology Branch
Project No. 1534 - Raid Fogger Plus
Application for Registration as Room
Fogger for Roaches, Fleas, etc.
(S.C. Johnson and Son, Inc.) - Review
of Seven Acute Studies

TOX Chem No. 652C

FROM: David G. Van Ormer, Ph.D.
Section III, Toxicology Branch
Hazard Evaluation Division (TS-769C)

DVO 17 Oct 86

TO: Arturo E. Castillo, PM 17
Insecticide-Rodenticide Branch
Registration Division (TS-767C)

THRU: Marcia van Gemert, Ph.D.
Head, Section III
Toxicology Branch
Hazard Evaluation Division (TS-769C)

M. van Gemert 10/20/86

and

Theodore Farber, Ph.D.
Chief, Toxicology Branch
Hazard Evaluation Division (TS-769C)

*W. Farber
10 21 86*

The six acute studies submitted are acceptable. The remaining data gap for Toxicology Branch (TB) approval of the subject registration is a 21-day inhalation study (on technical fenoxycarb) for which the test material particle size should have a mass median aerodynamic diameter of 1 um.

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Summary of toxicity parameters from data reviewed in this action:

| | <u>Tox. Category</u> |
|--|----------------------|
| 1. Acute oral LD ₅₀ , rat (both sexes) = greater than 5.0 g/kg. | IV |
| 2. Acute dermal LD ₅₀ , rabbit (both sexes) = greater than 2.0 g/kg. | III |
| 3. Acute inhalation LC ₅₀ , rat (both sexes, 4-hour, whole body) = 6.7 mg/L. | III |
| 4. Primary eye irritation, rabbit: irritation clearing in 7 days or less. | III |
| 5. Primary dermal irritation, rabbit: PII = 3.4 (moderately irritating). | III |
| 6. Dermal sensitization, guinea pig: negative for dermal sensitization when applied neat to female guinea pigs by modified Buehler test. | |

Exposure Scenario

The subject product is a pressurized solvent-based room fogger intended to produce a spray of small particles which will remain suspended for an extended time. The product is stated as providing "flushing, knockdown and kill" and "residual growth regulant" of many adult and recently hatched insects, particularly roaches and fleas. A 7.5 oz can is stated as being able to treat a room of up to 3000 cu ft of unobstructed space, and is intended for use in homes, apartments, and restaurants. Prior to release of spray, all food utensils are to be covered, pets removed, and waxed floors and furniture protected. Cupboards and cabinets should be opened, and the room closed off. All electrical appliances are to be disconnected and pilot lights extinguished. Only one can is to be used per room, which must be vacated for at least 2 hours. After treatment, the room is to be ventilated before reentry.

Data Requirements

The studies required to support the subject registration are as follows:

Acute Oral Toxicity;
Acute Dermal Toxicity;
Acute Inhalation Toxicity;

Primary Dermal Irritation;
Primary Eye Irritation; and
Dermal Sensitization.

All of the above studies are to be performed on both technical fenoxycarb and the subject formulation. The following studies are to be performed on technical fenoxycarb:

Teratogenicity (2 species);
Mutagenicity Battery;
90-Day Oral Feeding;
21-Day Dermal; and
21-Day Inhalation.

All of the above data requirements are on file in TB except for the 21-day inhalation study on fenoxycarb technical.

Consideration of the other three active ingredients of the subject formulation* leads TB to state that the pattern of use intended for the subject formulation does not differ significantly from existing uses of these chemicals.

[REDACTED] have been cleared for use on food crops according to 40 CFR 180.1001. (Food uses are not part of the subject exposure scenario.)

Label Evaluation (FR 49/188; Wednesday; September 26, 1984; p. 37981 ff.). Precautionary Statements for Inhalation Category III and for Dermal Category III should conform more closely to the required statements.

Use Classification (FR 40/129; July 3, 1975; pp. 28283-4). The subject formulation satisfies the criteria for General Use, Domestic.

*Pyrethrins, piperonyl butoxide, and N-octyl bicycloheptene dicarboximide.

INERT INGREDIENT INFORMATION IS NOT INCLUDED

Reviewed By: David G. Van Ormer, Ph.D.
Section III, Toxicology Branch (TS-769C)
Secondary Reviewer: Marcia van Gemert, Ph.D.
Section III, Toxicology Branch (TS-769C)

DVO 17 Oct 86 5549
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M. van Gemert 10/20/86

DATA EVALUATION REPORT

Study Type: Acute Inhalation - Rat -
(preliminary study)

TOX. Chem. No.: 652C

MRID No.: N/A

Accession No.: 261392

Test Material: Raid Fogger Plus

Active Ingredients: Pyrethrins 0.5%; piperonyl butoxide 1.0%;
N-octyl bicycloheptene dicarboximide
1.67%; fenoxycarb 0.6%

Inerts: [REDACTED]

Study No.: FDRL No. 7876

Sponsor: S.C. Johnson and Son, Inc.

Testing Facility: Food and Drug Research Laboratories, Inc.

Title of Report: Acute Inhalation Toxicity of 5826D14-1
in Sprague-Dawley Rats

Authors: B. Busch, J.A. Biesemeier, and P.J. Becci

Report Issued: October 15, 1984

Conclusions:

At an average aerosol concentration of 5.1 mg/L (analytical), four Sprague-Dawley rats (1/5 males, 3/5 females) succumbed within 15 days after a 4-hour, whole-body inhalation exposure. The animals exhibited labored breathing, decreased activity, and (in those succumbing) tremors, ataxia, and diarrhea. Necropsy showed reddened nasal passages and lungs in one or two animals.

Classification: Supplementary Data.

A. Materials:

The test formulation, in individual pressurized aerosol spray cans, was described by the sponsor as 5826D14-1. It was assigned FDRL ID No. 83-0880. The cans were shaken vigorously immediately before use.

The test animals were five male and five female albino rats, approximately 8 weeks of age (210 to 294 g) of the Sprague-Dawley derived strain from Charles River Breeding Laboratories, Wilmington, Mass. The animals were acclimated for a minimum of 5 days. Except during exposure, the animals were provided ad libitum with NIH 07 Open Formula certified rodent diet, and fresh tap water.

B. Methods:

The ten animals, selected randomly from an acclimated group, were exposed in individual cages to the test material aerosol for 249 minutes, including a 9-minute period to allow ~~the animals~~ approach to desired concentration.

close.

The exposure system consisted of a 128-L acrylic (Plexiglass) chamber, through which the total airflow was 65 L/min (transvector jet with pressure gauge). The test atmosphere was vented through a system constructed of a glass fiber prefilter, an HEPA filter and an activated charcoal bank. The test material was delivered to the chamber directly from the spray cans, operated manually for 10 seconds per minute. Intervals between activation were adjusted to establish the desired nominal chamber concentration of test material. Delivery to the chamber was through an air inlet port, which the Report describes as permitting the test material to mix with incoming air before being drawn down over the animals. Chamber temperature and relative humidity were measured twice per hour.

Nominal concentration (test material consumed divided by total volume of air) was 109.7 mg/L. Gravimetric concentration, determined twice each hour by drawing a known volume of chamber air through a preweighed glass fiber filter (Gelman Type A/E, 25 mm, 99.7% efficient at 0.3 μ m), was reported as an average of 0.5 mg/L. The actual concentration of test material was 5.1 mg/L, determined by extraction from the filters with isopropanol, followed by GC determination of ~~the~~^{the} active ingredient. Results were corrected by factors obtained from recovery data.

Particle size analyses, performed twice per hour, utilized a multijet cascade impactor (Model 02-200, In-Tox Products). Seven stainless steel impaction stages of this filter were

followed by a final filter stage, fitted with a cellulose membrane filter (Gelman Type A/E, 47 mm, Triacetate, 99.7% efficient at 0.3 μ m). Chamber air was drawn through the impactor at 20 L/min. Particle size parameters were calculated from a logarithmic distribution curve constructed from the percent aerosol collected at each stage.

Animal Observations for signs and mortality were recorded twice daily for 14 days. Body weights were recorded just prior to exposure, and on Days 8 and 15.

Gross pathology of all animals included examination of external surfaces and orifices, major visceral organs, and body cavities. Any lesions or abnormalities were recorded.

C. Results:

The Report notes that the average actual concentration of test material in the atmosphere was only 5 percent of the nominal concentration. This discrepancy was attributed to adsorption on chamber and animal surfaces, and the settling of larger particles. The fact that the gravimetric concentration was 10 percent of the actual concentration was attributed to evaporation of volatile components. The mean particle size (MMAD) was 13 μ m.

Mortality data are as follows:

| | Cumulative Mortality on Day | | |
|---------|-----------------------------|-----|------|
| | 1 | 2 | 3-15 |
| Males | 0/5 | 0/5 | 1/5 |
| Females | 1/5 | 1/5 | 3/5 |

The animals' coats were wet, suggesting dermal and oral exposure during the early phase of the test. All animals exhibited labored breathing and gasping, which subsided in survivors by Day 5. Decreased activity levels (all males, 3 females) returned to normal by Day 5. Other signs (occurring only in those succumbing) included tremors, ataxia, diarrhea, and hypothermia. There was a transient body weight decrease in two males and one female on Day 4.

The Report states that there were no lesions or abnormalities in any animal at termination. Necropsy findings for animals which died included darkened or reddened liver and lungs (in one and two animals, respectively), possibly due to postmortem tissue changes, according to the Report. The nasal passages of two animals were reddened. Adrenal glands were enlarged in one animal.

INERT INGREDIENT INFORMATION IS NOT INCLUDED

DVO Oct 3, 1986 005549

Reviewed By: David G. Van Ormer, Ph.D.
Section III, Toxicology Branch (TS-769C)
Secondary Reviewer: Marcia van Gemert, Ph.D. *Approved 10.9.86*
Section III, Toxicology Branch (TS-769C)

DATA EVALUATION REPORT -

Study Type: Acute Oral Toxicity - Rat TOX. Chem. No.: 652C

Accession No.: 261392 MRID No.: N/A

Test Material: Raid Fogger Plus

Active Ingredients: Pyrethrins 0.5%; piperonyl butoxide 1.0%;
N-octyl bicycloheptene dicarboximide
1.67%; fenoxycarb 0.6%

Inerts: [REDACTED]

Study No.: FDRL No. 7876B

Sponsor: S.C. Johnson and Son, Inc.

Testing Facility: Food and Drug Research Laboratories, Inc.

Title of Report: Acute Oral Toxicity in Rats

Authors: E.L. Reagan and P.J. Becci

Report Issued: December 16, 1983

Conclusions:

Classification: Guideline Data.

Acute oral LD₅₀, rat (male and female) = greater than 5.0 g/kg.

Toxicity Category: IV.

Signs: Decreased activity, ataxia, salivation, rales, nasal discharge, and diarrhea.

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A. Materials and Methods:

The test material is identified both as S.C. Johnson and Son, Inc., product No. 5826D14-3, and as FDRL ID No. 83-0881. The study utilized five male and five female young adult Sprague-Dawley rats (Charles River Breeding Laboratories, Inc., Wilmington, MA). Individually housed in an environmentally controlled room (with feed and water ad libitum), the animals were acclimatized for at least 5 days.

A single oral dose of 5.0 g/kg (at constant concentration) was administered after overnight fast. Observations were frequent on the day of dosing and twice daily through termination (Day 15). Body weights were recorded initially and at Day 8 and Day 15 (or at death). All animals were submitted for gross necropsy.

B. Results:

There were no deaths. Signs included decreased activity and ataxia in most of the animals, and fewer observations of salivation, rales, nasal discharge, and diarrhea. Gross necropsy indicated "no noteworthy findings."

Mean body weights increased 31 percent in males and 12 percent in females.

The acute oral LD₅₀ rat (male and female) is indicated as greater than 5.0 g/kg, with a 95 percent confidence level of 0 to 27 percent (E.L. Crow, Biometrika 43:423, 1956).

INERT INGREDIENT INFORMATION IS NOT INCLUDED

DVO 10-03-86

005549

Reviewed By: David G. Van Ormer, Ph.D.
Section III, Toxicology Branch (TS-769C)
Secondary Reviewer: Marcia van Gemert, Ph.D.
Section III, Toxicology Branch (TS-769C)

M. van Gemert 10.9.86

DATA EVALUATION REPORT

Study Type: Acute Dermal Toxicity -
Rabbit

TOX. Chem. No.: 652C

Accession No.: 261392

MRID No.: N/A

Test Material: Raid Fogger Plus

Active Ingredients: Pyrethrins 0.5%; piperonyl butoxide 1.0%;
N-octyl bicycloheptene dicarboximide
1.6%; fenoxycarb 0.6%

Inerts: [REDACTED]

Study No.: FDRL No. 7876B

Sponsor: S.C. Johnson and Son, Inc.

Testing Facility: Food and Drug Research Laboratories, Inc.

Title of Report: Acute Dermal Toxicity Study in Rabbits

Authors: E.L. Reagan and P.J. Becci

Report Issued: December 22, 1983

Conclusions:

Classification: Guideline Data.

Acute dermal LD50 rabbit (male and female) = greater than
2.0 g/kg.

Toxicity Category: III.

Signs: Dry, flaking skin; soft stools, anorexia.

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A. Materials and Methods:

The test material is identified both as S.C. Johnson and Son, Inc., Product No. 5826D14-3, and as FDRL ID No. 83-0881.

The study utilized five male and five female young-adult New Zealand White rabbits (New York State Rabbit Development, Hartwick, NY) individually housed in environment-controlled rooms. NIH Animal Feed A (certified) and water were provided ad libitum. The animals, identified by cage cards and ear tags were acclimated for a minimum of 5 days, during which time health examinations were conducted.

Fur clipping with electric clippers was performed on the day prior to dosing. The undiluted test material was administered to the intact skin of each animal at a level of 2.0 g/kg. The test area was covered with an occlusive binder (plastic wrap and stockinette sleeve) secured with masking tape.

The binders were removed after 24 hours in order to gently wipe away nonabsorbed test material. Observations were frequent on day of dosing, and twice daily through termination (Day 15). Body weights were recorded initially and on Days 8 and 15 (or at death). All animals, including those succumbing, were submitted to gross necropsy.

B. Results:

There were no deaths. Body weights showed slight increases in both sexes. Observations included dry, flaking skin in all animals, and fewer observations of soft stools and anorexia. Gross necropsy showed "no noteworthy findings."

The acute dermal LD₅₀, rabbit (male and female) was considered greater than 2.0 g/kg.

INERT INGREDIENT INFORMATION IS NOT INCLUDED

DVD 10-03-86 005549

Reviewed By: David G. Van Ormer, Ph.D.
Section III, Toxicology Branch (TS-769C)
Secondary Reviewer: Marcia van Gemert, Ph.D. *M. van Gemert 10.9.86*
Section III, Toxicology Branch (TS-769C)

DATA EVALUATION REPORT

Study Type: Acute Inhalation - Rat TOX. Chem. No.: 652C

Accession No.: 261392 MRID No.: N/A

Test Material: Raid Fogger Plus

Active Ingredients: Pyrethrins 0.5%; piperonyl butoxide 1.0%;
N-octyl bicycloheptene dicarboximide
1.67%; fenoxycarb 0.6%

Inerts: [REDACTED]

Study No.: FDRL No. 8349

Sponsor: S.C. Johnson and Son, Inc.

Testing Facility: Food and Drug Research Laboratories, Inc.

Title of Report: Acute Inhalation LC50 Study of 5826D14-1
Using Sprague-Dawley Rats

Authors: B. Busch, J.A. Biesemeier, and P.J. Becci

Report Issued: May 20, 1985

Conclusions:

| | | <u>95% C.L.</u> | <u>Slope</u> |
|--|-----------------------|-----------------|--------------|
| Acute 4-hour LC50 (whole body exposure) | 6.5 mg/L (males) | 5.2-7.7 | 15.0 |
| | 6.9 mg/L (females) | 4.4-9.4 | 4.8 |
| | 6.7 mg/L (both sexes) | 5.3-8.0 | 8.5 |

Toxicity Category: III

Significant Signs: Alopecia, decreased activity, labored breathing, nasal discharge, salivation, and tremors.

Body weight decrease in males.

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Six succumbing animals displayed reddened lungs and nasal passages or (mainly at top dose) corneal opacity.

Classification: Minimum Data.

A. Materials:

The test material was received in two shipments, identified as FDRL ID Nos. 84-0858 and 85-0144, contained in 33 individually pressurized aerosol spray cans. Each can was shaken vigorously before use, according to the report.

The Sprague-Dawley rats (Charles River Breeding Laboratories) were individually housed, with feed (NIH 07 Open Formula) and fresh tap water available ad libitum except during exposure. Acclimation and observation were for a minimum of 5 days prior to exposure. Identification was by ear notch and cage tag.

B. Methods:

Five male and five female rats per dose group were exposed to liquid droplet aerosols containing either 4.7, 7.2, or 8.3 mg/L (average analytical concentration) for 4 consecutive hours. A control group of five animals per sex were exposed to air only under the same exposure conditions.

The animals were exposed for 260 minutes in cages, placed at "mid-height" of a 128-liter acrylic chamber. Test material from a spray can, attached at an air inlet at the bottom of the vessel, was drawn through the chamber by means of a transvector jet, and vented via an air treatment system consisting of a glass fiber prefilter, an activated charcoal bank, and an HEPA filter. Air flow was 30 L/minute.

Nominal concentration was calculated as utilized test material divided by total air volume passing through. Gravimetric concentration was calculated from the change in weight of a glass fiber filter (Gelman Type A/E, 99.7% efficient at 0.3 μ m) and the volume of chamber air sampled through the filter. Sampling frequency was every half hour. Each filter was then submitted to chemical analysis to determine the actual analytical concentration. Filter extracts (isopropanol) were quantified by gas chromatography, corrected by recovery-tests.

Particle size analysis, performed twice per hour, utilized a multijet cascade impactor (Model 02-200, In-Tox Products). The first seven stages of the impactor contained preweighed stainless steel impaction substrates. The final (eighth)

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stage contained a cellulose filter membrane (Gelman A/E, 47 mm, Triacetate, 99.7% efficient at 0.3 μ m). The impactor received chamber air at 20 L/minute. A distribution curve was plotted for cumulative percent aerosol collected at each stage. Readings of chamber temperature and relative humidity were taken at 30-minute intervals.

The animals were observed for signs twice daily during the 14-day observation. Body weights were recorded on Days 1, 4, 8, and 15. All animals were subjected to gross pathology.

The LC₅₀ calculations, based on analytical concentrations, were performed by the method of Miller and Tainter (1944). Change in body weight was analyzed by a one-way ANOVA, with differences from control identified by the Least Significant Difference Test. Incidence data were analyzed using Fisher's Exact Test, with significance judged at $p < 0.05$.

C. Results:

The mean analytical concentration was only 2 to 3 percent of the nominal concentration. The Report notes that surface adsorption to chamber and animals, as well as particle settling, contributed to this difference. Gravimetric concentrations were 12 to 15 percent of the analytical values, and are expected to be less, due to solvent evaporation.

The particle size (mass median aerodynamic diameter [MMAD]) ranged from 5.8 to 7.0 μ m for the three dose groups, according to the report. Chamber temperature was 17 to 24 °C, and relative humidity ranged from 30 to 64 percent.

Mortality is summarized as follows:

| Analytical Concentration (mg/L) | Percent Mortality | | |
|------------------------------------|-------------------|---------|----------|
| | Males | Females | Combined |
| 4.7 | 0 | 20 | 10 |
| 7.2 | 60 | 60 | 60 |
| 8.3 | 100 | 60 | 80 |

Results of LC₅₀ calculation are as follows:

| | Males | Females | Combined |
|-------------------------|---------|---------|----------|
| LC ₅₀ (mg/L) | 6.5 | 6.9 | 6.7 |
| 95% Conf. limits | 5.2-7.7 | 4.4-9.4 | 5.3-8.0 |
| Slope | 15.0 | 4.8 | 8.5 |

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Significant Signs:

Alopecia - males at mid dose,
females at mid and top dose.

Decreased activity - males at the two low doses,
females at all doses.

Nasal discharge - males at the two low doses,
females at all doses. Dark material
around nose of females at top dose.

Labored breathing, rales - males at the two low doses,
females at all doses.

Salivation - females at top dose.

Tremors - males at mid dose.

Wet coats of surviving animals indicated dermal absorption.

Body weight changes, compared to controls, were decreased for males at low dose on Days 4 and 8, and at mid dose on Day 4. (All males succumbed at top dose.)

Gross necropsy examination revealed no abnormalities in survivors, according to the Report. Among animals that died there were bright- or dark-red lungs (one female at low dose, two of each sex at mid dose). Bright-red nasal passages occurred in one female at mid dose. Corneal opacity was noted in one female at mid dose and in five animals at top dose.

A preliminary screening study (FDRL No. 7876) resulted in one male and three female deaths after five rats of each sex were exposed to an aerosol of 5.1 mg/L for 4 hours and observed for 14 days.

INERT INGREDIENT INFORMATION IS NOT INCLUDED

005549

DVO 10-03-86

Reviewed By: David G. Van Ormer, Ph.D.
Section III, Toxicology Branch (TS-769C)
Secondary Reviewer: Marcia van Gemert, Ph.D. *M van Gemert 10.9.86*
Section III, Toxicology Branch (TS-769C)

DATA EVALUATION REPORT

Study Type: Primary Dermal Irritation - Rabbit TOX. Chem. No.: 652C

Accession No.: 261392 MRID No.: N/A

Test Material: Raid Fogger Plus

Active Ingredients: Pyrethrins 0.5%; piperonyl butoxide 1.0%;
N-octyl bicycloheptene dicarboximide
1.67%; fenoxycarb 0.6%

Inerts: [REDACTED]

Study No.: FDRL No. 7876B

Sponsor: S.C. Johnson and Son, Inc.

Testing Facility: Food and Drug Research Laboratories, Inc.

Title of Report: Primary Dermal Irritation Study in Albino Rabbits

Authors: E.L. Reagan and P.J. Becci

Report Issued: February 15, 1984

Conclusions:

Classification: Guideline Data.

PII = 3.4 Moderately Irritating; Toxicity Category III.

005549

A. Materials and Methods:

The test material is identified both as S.C. Johnson and Son, Inc. Product No. 5826D14-3, and as FDRL ID No. 83-0881.

The study utilized six young adult New Zealand White rabbits (unstated sex) from New York State Rabbit Development, Hartwick, NY. Individually housed in an environment-controlled room, the animals received NIH Animal Feed A (certified) and water ad libitum. Identification was by ear tag and cage card, and acclimatization was for at least 5 days, during which time the animals received health status examinations.

The back of each rabbit was shaved free of fur with electric clippers (avoiding abrasion) on the day prior to dosing. A volume of 0.5 mL of undiluted test material was applied to each of two test sites on either side of the spinal column. Each site was then occluded with a 1-inch-square gauze patch and Blenderm[®] tape.

After a 4-hour exposure period the test sites were gently wiped to remove residual test material, and then examined and scored separately for erythema and edema on a graded scale of 0 to 4 (Draize, Woodard et al., 1944). Subsequent scoring periods were at 28, 52, 76 hours; and 4, 7, 10, and 14 days postexposure.

Calculation of the Primary Irritation Index (PII) was as follows: scores at the 28-, 52-, and 76-hour evaluations for erythema (and eschar) were added to scores for edema at the same periods to yield a total, which was divided by six (accounting for left and right test sites) to produce each individual animal score. The PII was then calculated as the mean of the total scores for the six rabbits.

B. Results:

PII = 3.4 Moderately Irritating.
(J. Soc. Cosmet. Chem. 13:281, 1962).

Toxicity Category: III.

INERT INGREDIENT INFORMATION IS NOT INCLUDED

DVO 10-03-86 005549
Management 10.9.86

Reviewed By: David G. Van Ormer, Ph.D.
Section III, Toxicology Branch (TS-769C)
Secondary Reviewer: Marcia van Gemert, Ph.D.
Section III, Toxicology Branch (TS-769C)

DATA EVALUATION REPORT

Study Type: Primary Eye Irritation -
Rabbit

TOX. Chem. No.: 652C

Accession No.: 261392

MRID No.: N/A

Test Material: Raid Fogger Plus

Active Ingredients: Pyrethrins 0.5%; piperonyl butoxide 1.0%;
N-octyl bicycloheptene dicarboximide
1.67%; fenoxycarb 0.6%

Inerts: [REDACTED]

Study No.: FDRL No. 7876B

Sponsor: S.C. Johnson and So., Inc.

Testing Facility: Food and Drug Research Laboratories, Inc.

Title of Report: Primary Eye Irritation Study in Rabbits

Authors: E.L. Reagan and P.J. Becci

Report Issued: December 13, 1983

Conclusions:

Classification: Guideline Data.

Toxicity Category: III (Irritation clearing in 7 days or less).

005549

A. Materials and Methods:

The test material is identified both as S.C. Johnson and Son, Inc. Product No. 5826D14-3, and as FDRL ID No. 83-0881.

The six young adult New Zealand White rabbits (New York State Rabbit Development, Hartwick, NY) were individually housed in an environment-controlled room, and provided with NIH Animal Feed A (certified) and water ad libitum. During the 5-day acclimatization the rabbits were examined daily for general health. Identification was by cage card and ear tag. The eyes of the rabbits, prior to dosing, were examined for irritation and lesions by sodium fluorescein/UV.

Administration was by spray can held 10 cm from the eye and sprayed for 1 second, the other eye serving as control. With fluorescein examination the eyes were graded for ocular reaction at 1, 24, 48, and 72 hours postdosing, by use of the Draize scale for ocular lesions. If necessary, further examination for persisting injury was conducted at Day 4 and every 3 days thereafter until reversal of irritation, or until Day 21.

B. Results:

At 1 hour postdosing the total scores for the six animals were 2, 2, 2, 2, 6, and 11. At 24 hours the respective scores were 0, 0, 0, 2, 0, and 2. At all later periods all responses were tabulated as zero for all animals.

Toxicity Category: III (Irritation clearing in 7 days or less).

INERT INGREDIENT INFORMATION IS NOT INCLUDED

Reviewed By: David G. Van Ormer, Ph.D.
Section III, Toxicology Branch (TS-769C)
Secondary Reviewer: Marcia van Gemert, Ph.D.
Section III, Toxicology Branch (TS-769C)

DVO 10-03-86 005549
M van Gemert 10-9-86

DATA EVALUATION REPORT

Study Type: Dermal Sensitization - Guinea Pig

TOX. Chem. No.: 652C

Accession No.: 261392

MRID No.: N/A

Test Material: Raid Fogger Plus

Active Ingredients: Pyrethrins 0.5%; piperonyl butoxide 1.0%;
N-octyl bicycloheptene dicarboximide 1.67%; fenoxycarb 0.6%

Inerts: [REDACTED]

Study No.: FDRL No. 8349

Sponsor: S.C. Johnson and Son, Inc.

Testing Facility: Food and Drug Research Laboratories, Inc.

Title of Report: Dermal Sensitization Study of 5826D14-1 in Albino Guinea Pigs (Modified Buehler Test)

Authors: E.L. Reagan and P.J. Becci

Report Issued: January 7, 1985

Conclusions: Negative for dermal sensitization when applied neat to female guinea pigs by modified Buehler test.

Classification: Guideline Data.

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A. Materials:

The test material is identified both as ID No. 5826D14-1 and as FDRL ID No. 84-0858. The positive control was 1-chloro-2,4-dinitrobenzene (DNCB) from Fisher Scientific. These chemicals were stored at ambient room temperature.

The test animals were young adult female albino guinea pigs, 4 to 12 weeks of age (Hartley-derived strain) from Buckshire Corp. The animals were observed daily for general health during a 5-day acclimation. NIH Animal Feed A and fresh tap water were available ad libitum. The animals were identified by ear notching and cage tag, and were housed individually under environment-controlled conditions, with a 12/12 light/dark cycle. Ten guinea pigs comprised the test group, with six in the positive control groups (for both induction and challenge phases). Three additional naive animals were used for naive challenge control.

B. Protocol:

The Report designates the protocol as a modified Buehler test. The study consists of the dermal exposure of ten female guinea pigs to ten dermal applications (induction series) of 0.5 mL of neat test material. The applications are spaced at 3X per week and are located at rotating test sites on the animal. Each induction application lasts 6 hours under wrapped patches, on sites shaved the day prior to treatment. Positive control (0.07% DNCB in 70% ethanol) was applied by similar protocol to 10 animals.

After a 2-week rest period, the animals were challenged by an eleventh exposure to test material at a virgin site. Three additional, naive animals (as challenge control) were concurrently initially exposed, similarly to the eleventh application for the treated animals. Positive control challenge was with 0.07% DNCB in acetone, with separate acetone controls (3 animals).

Both induction and challenge application sites were examined and evaluated for dermal irritation at 24 and 48 hours. The animals were observed daily for signs. Initial and final body weights were recorded.

Statistical analysis of dermal response scores was by the Mantel-Haenszel Procedure, according to the Report. Challenge scores were compared to both control scores and to initial (Day 1) scores of the induction series.

C. Results:

A prior range-finding study involved four female guinea pigs, each of which received dermal application of four concentrations (0.5 mL each, at four separate sites) of test material in mineral oil: 25, 50, 75, and 100% (w/v). These applications were made on Days 1 and 4. Since there was no dermal irritation at any concentration in any of the four animals, the neat test material was chosen as the test concentration for the main study.

During the main study all animals appeared normal, according to the Report. Differences in mean body weight gain appear not treatment-related.

Erythema Response: At the ten observation periods the mean induction erythema scores ranged from 0 to 0.5 at both 24 hours and 48 hours, while the mean positive control scores ranged from 0.2 to 2.5 at 24 hours and 0.2 to 2.0 at 48 hours.

Challenge erythema scores are listed as zero for all treated animals at both 24 hours and 48 hours. Naive control and acetone challenge scores also are zero, while mean positive control scores for challenge are tabulated as 2.0 at 24 hours, and 2.5 at 48 hours. These positive control scores are both listed in the Report as significantly different ($p < 0.05$) from the first positive control induction response.

Edema Response: For all treated animals (at either 24 hours or 48 hours) both the induction and challenge edema scores are zero. The only edema responses of the study are in the positive controls grouped near the mid point of the study (0.2 to 0.5; 24 hours and 48 hours), and also in the positive control challenge at 48 hours (score 0.3).

D. Summary:

Negative for dermal sensitization when applied neat to female guinea pigs by modified Buehler test.