E. Safety

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2. Summary of Safety Data

a. Petitioner's Appraisal of Safety Data

The 90-day subacute oral toxicity data on albino rats indicates that, at the 100 and 300 ppm levels in the diet, no adverse effects were found. The 18-week subacute toxicity study in white Leghorn chickens indicates that a no-effect level was 500 ppm, with the minor exception of slightly reduced body weights at all levels in male birds. Finally, no chick edema factor was present in testing terphenyl chlorinated to 60 weight percent in white Leghorns for 21 days at doses of 50, 200 and 400 ppm.

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b. Petitioner's Conclusion

With a no-effect level at or slightly above 300 ppm, combined with the utilization of a functional barrier between the adhesive containing terphenyl chlorinated to 60 weight percent, this use should present no toxicity problem or hazard. The margin of safety should be more than adequate.

3. Analysis and Interpretation of Safety Data

(a) 90-day Subacute Oral Toxicity to Albino Rats (Appendix - Exhibit 3)

Eighty rats (40 male and 40 female) were used in the experiment. Ten each were fed separately at either 100, 300 or 1,000 ppm with 10 each serving as controls. Results are as follows:

(1) Body Weights and Weight Gains

Animals in the 100 and 300 ppm levels exhibited growth patterns similar to the controls. Animals in the 1,000 ppm level exhibited slight growth depression which was not confirmed statistically at the conclusion of the study.

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(2) Food Consumption

Animals in the 100 and 300 ppm levels ate amounts of food essentially comparable to that eaten by the controls. Food consumption among animals in the 1,000 ppm group was somewhat lower than the controls.

(3) Mortality and Reactions

Five animals died during the investigation: a control male on day 15 of acute respiratory infection; a control female on day 30 - no cause was determined; two 300 ppm animals died of pneumonia on days 55 and 63 respectively; one 1,000 ppm female on day 89 as a result of trauma incurred during the collection of blood samples.

No untoward behavioral reactions were noted among any of the animals employed in the study.

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(4) Hematologic Studies

No significant differences in results between test animals and controls were noted during the studies.

(5) Clinical Blood Chemistry Studies

Values obtained for the test animals were comparable to the controls.

(6) Urine Analysis

No difference between the urine of test animals and the controls was detected.

(7) Pathologic Studies

Gross Pathologic Findings - Gross pathologic findings among test rats were comparable to controls.

Organ Weight and Ratio Data - A few intergroup differences were noted: liver weights and ratios were elevated among animals in the 1.000

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ppm level as was the liver to body weight ratio of males in the 300 ppm group. Females in the 100 ppm group exhibited a dimunition of spleen to body and spleen to brain weight ratios but this was not seen at the 300 or 1,000 ppm levels.

(8) Microscopic Pathologic Findings

Findings among animals in the 1,000 ppm group were comparable to those noted in the controls.

(b) 18-week Chicken Toxicity (Appendix - Exhibit 4)

Four male and twenty female white Leghorns were separately tested at 500, 1,000 and 2,000 ppm. Four male and twenty females were used as controls.

The results follow:

(1) Body Weight Data

The body weights of the female birds at all test levels compared favorably with the controls. The body weights of the male

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birds in the test groups were slightly lower than those in the control.

(2) Food Consumption Data

Food consumption in the 500 and 2,000 ppm birds was comparable to the controls. The 1,000 ppm birds consumed less food, especially during the last two measurements.

(3) Behavioral Reactions

There were no abnormal behavioral reactions noted among the birds in any of the groups tested.

(4) Mortality Data

The 500 ppm birds were similar to the controls in their mortality data. However, there was a drug-related effect on mortality at the higher dose levels (at 1,000 and 2,000 ppm).

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(5) Egg Production and Egg Weight Data

The number of eggs collected and the average weight of eggs in the 500 ppm group compared favorably with the controls. Egg production was depressed in the 1,000 and 2,000 ppm groups due to increased mortality. Also egg weight data was lower in the 2,000 ppm group.

(6) Gross Pathologic Findings

The contents of the gizzard in many of the test birds were green in color. The other findings were of a spontaneous nature.

(c) 21-Day Chick Edema (Appendix - Exhibit 5)

Twelve white Leghorns each were used for testing at 50, 200 and 400 ppm. Twelve birds were also used as controls. Results follow:

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(1) Mortality and Reactions

No deaths or abnormal behavioral reactions were noted during the test period.

(2) Body Weight Data

Body weights in the 50 and 200 ppm birds were slightly above those of the controls, while the birds at 400 ppm showed slightly reduced body weights.

(3) Subcutaneous or Peritoneal Edema

No evidence of either edema was found during autopsy of the test birds.

(4) Pericardial Edema

The mean at 200 ppm was 0.21 ml, while the means at 50 and 400 ppm were 0.19 ml and the control was 0.15 ml. No significant increase in edema was noted.

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(5) Gross Pathologic Findings

No significant gross pathologic alterations were noted in the tissues and organs examined from any of the test animals.

4. Raw Safety Data

(a) 90-day Subacute Oral Toxicity in Albino Rats

Appendix - Exhibit 3

(b) 18-week Subacute Toxicity in Chickens

Appendix - Exhibit 4

(c) 21-day Chick Edema Studies

Appendix - Exhibit 5

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APPENDIX

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