MEMORANDUM

JUL 20 1986

SUBJECT: Review of Subchronic Inhalation Study in Rats with Endosulfan

TO: George LaRocca, PM 15
Registration Division (TS-767)

FROM: Margaret L. Jones
Review Section III
Toxicology Branch (TS-769)

THROUGH: Marcia Van Gemert, Ph.D., Head
Review Section III
Toxicology Branch

and Theodore M. Farber, Ph.D., Chief
Toxicology Branch

Compound: Endosulfan

Registration No. 154123

Accession No: 256115, 256126

Tox. Project No: 489

Registriant: American Hoechst

Action Requested: Review the Subchronic inhalation study in rats which was submitted as follow-up data to the 1982 Endosulfan Registration Standard. Data on subchronic inhalation were listed as a data gap.

Conclusions: Ten male and 10 female SPF Wistar rats were administered 0, 0.0005, 0.0010, and 0.0020 mg Endosulfan/l air for 89 days. Air and vehicle controls were used. An additional 5 animals at each dose were held for a 4-week recovery period after receiving the test aerosol. The study apparently did not reach a maximum tolerated dose. Some slight effects on clinical chemistry and in hematology counts were noted but these do not demonstrate significant toxicity of the test compound.
Discussion of Selected Results and Deficiencies: Body weight in males was lowered 3-5% of the high dose from day 20-30. Lowered body weight was more pronounced in the high dose recovery group of 5 animals from day 31-60. However, since only 5 animals were held, the 12-14% lowering of body weight does not demonstrate significant toxicity and cannot be analyzed statistically in a meaningful way. Food consumption in males was lower than controls in the high dose group from day 20-30 and likewise in the 5 animals held through day 60. Again, the minimal lowering of food consumption in only 5 animals does not demonstrate significant toxicity of the test compound. Erythrocytes were significantly elevated in males in the low and mid dose groups at the end of exposure (29 days). This effect is apparently spurious, since it was not observed at the high dose. The changes discussed above do not demonstrate a pattern of toxicity clearly related to the test substance. In addition, the test report states the values were within the norm for the strain and species used, although no historical control data were included to support this statement.

Specific deficiencies in the test report are listed below:

1. The study fails to demonstrate a maximum tolerated dose for the test compound with clear signs of toxicity at the high dose.

2. Length of administration of test substance was not clearly stated in the test report. There are several indications the length of administration was 21 days although most of the information indicates it was 29. Since most of the results discussed above were observed between days 20-30, the length of administration is critical to evaluation of this study.

3. Statements about monitoring of temperature and humidity were misleading. The report states these parameters were monitored "continuously", however evidence in the tables indicates measurements were taken every 5-6 days for each group.

4. Historical control data are necessary to support the statements which indicate erythrocyte counts and other parameters were normal for the species and strain considered.
Reviewed by: Margaret L. Jones  
Section III, Tox. Branch (TS-769)  

Secondary reviewer: Marcia Van Gemert, Ph.D.  
Section III, Tox. Branch (TS-769)  

DATA EVALUATION REPORT  

Study Type: 21 Day Inhalation in the Rat  
Tox. Chem. No.: 420  

Accession Number: 256115, 256126  
MRID: none  

Test Material: Endosulfan  

Synonyms: Thiodan®, Thionex®  

Study Number(s): Report No: 84.0539 (Translation of Study No. 83.0103); [Doc. No. A 29823 (Translation of Doc. No. A29766)]  

Sponsor: American Hoechst  

Testing Facility: Hoechst Aktiengesellschaft, Pharma Forschung Toxikologie, Frankfurt, W. Germany  

Title of Report: Endosulfan-active ingredient technical (Code: NOE 02671 OI ZD 97 0003) Testing for Subchronic Inhalation Toxicity - 21 exposures in 29 days in SPF Wistar Rats  

Authors: Hollander, Weigand, Kramer  

Report Issued: 15 August 1984  

Conclusions: Ten male and 10 female SPF Wistar rats were administered 0, 0.0005, 0.0010, and 0.0020 mg Endosulfan/l air for 29 days. Air and vehicle controls were used. An additional 5 animals at each dose were held for a 4-week recovery period after receiving the test aerosol. The study apparently did not reach a maximum tolerated dose. Some slight effects on clinical chemistry and in hematology counts were noted but these do not demonstrate significant toxicity of the test compound.  

Classification: Core Unacceptable  

Discussion of Selected Results and Deficiencies: Body weight in males was lowered 3-5% at the high dose from day 20 through 30. Lowered body weight was more pronounced in the high dose recovery group of 5 animals from day 31-60. However, since only 5 animals were held, the 12-14% lowering of body weight does not demonstrate significant toxicity and cannot be analysed statistically in a meaningful way. Food consumption in males was lower than controls in the high dose group from day 20 through 30 and likewise in the 5 animals held through day 50. Again, the minimal lowering of food consumption in only 5 animals does not demonstrate significant...
toxicity of the test compound. Erythrocytes were significantly elevated in males in the low and mid dose groups at the end of exposure (29 days). This effect is apparently spurious, since it was not observed at the high dose. The changes do not demonstrate a pattern of toxicity clearly related to the test substance. In addition the test report states the values were apparently within the norm for the species and strain studied, although no historical control data were submitted to support this statement. Specific deficiencies in the test report are discussed below:

The following deficiencies were found in the test report:

1. The study fails to demonstrate a maximum tolerated dose for the test compound with clear signs of toxicity at the high dose.

2. Length of administration of test substance was not clearly or consistently stated in the test report. There are several indications the length of administration was 21 days although most of the information indicates it was 29. Since most of the results discussed above were observed between days 20-30, the length of administration is a critical factor in the evaluation of this study.

3. Statements about monitoring of temperature and humidity were misleading. The report states these parameters were monitored "continuously", however evidence in the tables indicates the measurements were taken every 5-6 days for each group.

4. Historical control data are necessary to support the statements which indicate erythrocyte counts and other parameters were normal for the species and strain considered.

A. Materials:

1. Test Compound: Endosulfan (6,7,8,9,10,10-Hexachloro-1,5,5a, 6,9,9a-hexahydro-6,9-methano-2,4,3-benzodioxathiepin-3-oxide); Brown flakes; Batch No. 002671 OI ZD 97 0003; 97.2% pure; contaminants not listed; Vehicle: Ethanol:polyethylene glycol 400 (1:1) administered with test substance and alone to vehicle controls; a one percent solution of the test substance with vehicle was prepared daily.

2. Test Animals: Wistar Rats, strain HOE: WISKr(SPF71) from Horhst AG, Pharma Forschung Toxikologie, Kastengrund, bred under "SFr" conditions; 5-7 weeks old at start of test substance administration; Males weighed 114-135 g., Females weighed 114-130 g.

B. Study Design:

1. Animal assignment: Animals were assigned randomly to the
toxicity of the test compound. Erythrocytes were significantly elevated in males in the low and mid dose groups at the end of exposure (29 days). The changes do not demonstrate a pattern of toxicity clearly related to the test substance. In addition the test report states the values were apparently within the norm for the species and strain studied, although no historical control data were submitted to support this statement. Specific deficiencies in the test report are discussed below:

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B. Study Design:

1. Animal assignment: Animals were assigned randomly to the following test groups and housed in groups of 5 animals per cage between exposures and one per cage during exposures:
<table>
<thead>
<tr>
<th>Test Group and Dose</th>
<th>29 admin. in 29 days</th>
<th>29 admin. + 1 week recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>male</td>
<td>female</td>
</tr>
<tr>
<td>Air Control (0)</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Vehicle Control (2 ml/L)</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Low (0.0005 mg a.i./L air)</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Mid (0.0010 mg a.i./L air)</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>High (0.0020 mg a.i./L air)</td>
<td>10</td>
<td>10</td>
</tr>
</tbody>
</table>

After apparently receiving 29 exposures in 29 days, 10 animals per group were sacrificed and 5 were held for an additional 1 week observation period. The animals sacrificed at 30 days were designated at the start of the study.

2. Exposure: Animals were exposed 6 hours/day, 5 days/week for a total of 21 (29) exposures (see comments below) by placing them "nose-only" in an 80 liter glass and stainless steel cylinder. The chamber stood in a vent pipe of 1 cubic meters volume with suction at the bottom to draw off excess aerosol.

Comment on length of exposure: The test report indicates three different lengths of exposure: the title states "21 exposures in 29 days"; p. 12 states "29 exposures in 29 days"; 22 readings were recorded during the exposure period. This review will refer to 29 exposures as the apparently correct length of time from the results section.

3. Animals received Altromin R124 pellets and water ad libitum, except during exposures.

4. Statistics: various methods were used to analyse the different data collected in this study: body weights- parametric method of Dunnett, and distributed-free method by Nemeyi/Dunnett; hematolgy- the above methods and parametric method by Sidak

5. Quality Assurance inspections were performed on both Report No. 83.0103 and its translation, No. 84.0539. Reports were made 4 times between 29 April 1983 and 21 September 1984.

C. Measurements:

All measurements were made in the breathing zone of the animals. Aerosol generation was performed under dynamic conditions. Air was provided at 800 l/hr by an air-calibrated rotameter. There were 10 air changes per hour. Slight negative pressure in the chamber was maintained by drawing out test atmosphere at the rate of 1100 l/hr. Nozzles of varying diameter were used to attain the concentrations of test substance: 0.1 mm for vehicle control, 0.3 mm for low dose, and 0.15 mm for mid and high dose groups. A one percent solution of the test substance was injected into the nozzle at a constant speed. Air flow was 3 l/min (1.25 m/sec). The measurement method for air flow was not specified.
a. **Gravimetric concentration** was measured using Sartorius Membranfilter GmbH (Gottingen) membrane filters 50 mm. in diameter with pore width 0.65 μm, once daily for vehicle controls and 3 times per day for the exposure groups, at the same time CO, CO₂, and O₂ were monitored.

b. **Chemical concentration** was measured by passing 18 liters of test atmosphere in 1 hour through gas washing bottles filled with acetone and placed in a cold methanol bath. Concentration of active ingredient was determined using gas chromatography. Samples were measured on days 2, 7, 14, 21, and 28.

c. **Particle size** was measured using a Model 225 Particle Counting System (Kratel GmbH, Gerlingen) once per hour in vehicle controls and in the exposure groups.

d. **CO, CO₂, O₂, temperature, and humidity** - CO, CO₂, and O₂ were measured at 30 minutes, 2 hours, and 4 hours during each exposure day. For the air only control group, these measurements were made on days 3 and 27 only. CO and CO₂ were measured with Uras 2T Infra Red Gas Analyser, O₂ with a Magnos 3 oxygen analyser, temperature with a CMR Messzumformer TBU 320, and atmospheric humidity with a Vaisala HMT 12 Transmitter.

**Results:**

a. **Gravimetric concentration:**

- 0.0005 mg a.i. = 44 mg of 1% solution/m³ air
- 0.0010 mg a.i. = 84 mg of 1% solution/m³ air
- 0.0020 mg a.i. = 167 mg of 1% solution/m³ air

Vehicle control = 246 mg ethanol-polyethylene glycol 400/m³ air

b. **Chemical concentration** - mean concentrations corresponding to the "ideal" ones above were:

- 0.00053 mg a.i. (for 0.0005 mg a.i. group)
- 0.00088 mg a.i. (for 0.0010 mg a.i. group)
- 0.00221 mg a.i. (for 0.0020 mg a.i. group)

c. **Particle size**: In all test groups, more than 90% of the particles were under 6 μm in diameter. More than 87% of particles in the vehicle control group were under 6 μm in diameter.

d. **CO, CO₂, O₂, temperature, humidity**: CO levels were 0-7 ppm; CO₂ ranged from approximately 3500 ppm-20000 ppm (3800-17000 for test groups, 5500-20000 for vehicle control, and 9600-11000 for air only control); O₂ content was close to 19% in test groups and air-only controls, and ranged from 18-20 in vehicle controls. Temperature was approximately 21-25°C*. Humidity ranged from 31-54% in test groups, 28-53% in vehicle control, and 37-43% in air-only controls.

* Temperature and humidity were monitored 3 times per day on 5-6 alternate days of the 29 day test period (approximately every 5 days for each group).
2. **Observations for toxicity and mortality:** Animals were inspected before the start of the test period, during exposure periods, and at the end of the study. They were examined weekly for neurological disturbances, changes in opacity of refracting media, lesions of the oral mucosa, and abnormalities in dental growth.

**Results:** No visible effects of the test compound were apparent upon observation of the majority of animals. One male in the high dose group demonstrated toxic signs consisting of emaciation, pale skin, squatting position and high-legged position from day 12 until the end of the study. No mortality occurred in the test period or in the recovery period.

3. **Body weight** was recorded twice weekly throughout the study. Ten animals from each group were sacrificed one day after the last exposure. The exact day of sacrifice of the original test group is not clear in the test report (day 22 or day 34, according to the information in the test report).

**Results:** Group mean body weights were similar to controls with the exception of high dose males from day 20 of the exposure period to day 30, whose weights were 3-5% lower than controls. In the 5 recovery males at this dose, body weights lagged approximately 50 g. (12-16%) behind controls and other groups from day 34 to day 60. Statistical analysis of recovery results would not be meaningful due to the small sample size.

There were apparently no compound related effects on body weight.

4. **Food consumption** was measured indirectly by biweekly weighing. **Water consumption** was measured biweekly in an unspecified manner.

**Results:** Food consumption was significantly decreased in high dose males on day 20. Food consumption for the recovery group averaged from 3-1/2 g/day less than controls during the recovery period, except for day 34, when food consumption was 15 g less than controls. Water consumption in vehicle controls and in male dose groups was slightly increased, compared to air-only controls.

There were apparently no compound related effects on food and water consumption.

5. **Food efficiency** was not reported. The calculation in only 5 animals was not considered meaningful by the reviewer.

6. **Hematology parameters** were examined one day after the last exposure in 10 animals from each group. Blood was withdrawn from the retrobulbar venous plexus. Parameters were again examined at the end of the recovery period in the 5 remaining animals from each group. Animals were sampled randomly to avoid systematic errors. The following parameters were measured or calculated from others:
Hemoglobin(Hb)
Reticulocytes
Hematocrit(HCT)
Leucocytes
Differential blood count
Thrombocytes
Coagulation time
Heinz bodies
Mean corpuscular volume (MCV)
Mean corpuscular hemoglobin (MCH)
Mean corpuscular hemoglobin concentration (MCHC)

Results: Significant changes in erythrocytes, leucocytes, hemoglobin, and hematocrit were noted upon statistical analysis, as follows:

Subchronic Inhalation with Endosulfan in Rats/Hematology

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Sex</th>
<th>Control</th>
<th>Vehicle</th>
<th>0.0005 mg/l</th>
<th>0.0010 mg/l</th>
<th>0.0020 mg/l</th>
</tr>
</thead>
<tbody>
<tr>
<td>One Day After End of Exposure (n=10)</td>
<td></td>
<td>(air)</td>
<td>(vehicle)</td>
<td>1 air</td>
<td>1 air</td>
<td>1 air</td>
</tr>
<tr>
<td>erythrocytes</td>
<td>M</td>
<td>7.62</td>
<td>7.91</td>
<td>8.48*</td>
<td>8.11*</td>
<td>8.11</td>
</tr>
<tr>
<td>(10^12/l)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>leucocytes</td>
<td>M</td>
<td>8.1</td>
<td>7.7</td>
<td>8.2</td>
<td>7.2</td>
<td>6.4*</td>
</tr>
<tr>
<td>(10^9/l)</td>
<td>F</td>
<td>5.6</td>
<td>7.5*</td>
<td>7.3</td>
<td>6.6</td>
<td>7.2</td>
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<tr>
<td>hemoglobin</td>
<td>M</td>
<td>156</td>
<td>163</td>
<td>172*</td>
<td>165</td>
<td>166</td>
</tr>
<tr>
<td>(g/l)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>hematocrit</td>
<td>M</td>
<td>0.43</td>
<td>0.44</td>
<td>0.46*</td>
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<td>0.45</td>
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<tr>
<td>(unity)</td>
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</tbody>
</table>

* Statistically significant difference in parameter as compared to air-only controls at p<0.05.

Although differences in some of the above parameters are statistically significant, most of the above changes do not appear to be dose or compound related. Although erythrocyte counts were significantly increased at the low and mid doses, the effect is apparently spurious, since it was not observed at the high dose. The decrease in leucocyte count in males seems to be marginally dose related. None of the changes appears to demonstrate significant toxicity of the test compound.

7. Clinical chemistry parameters were examined one day after the last exposure and at the end of the recovery period (29 more days). Blood was sampled from the retrobulbar venous sinus. Animals were then killed by cervical dislocation under Nembutal anaesthesia and exsanguinated. The following parameters were examined:
sodium
potassium
bilirubin, total and direct
creatinine
glucose
urea nitrogen
calcium
chloride
SGOT
SGPT
AP
cholesterol
total protein
methemoglobin
lactate dehydrogenase (LDH)

Results: Significant changes at the end of the exposure period in chloride, urea nitrogen, cholesterol, calcium, creatinine, and SGOT, and at 29 days after the end of exposure in glucose, urea nitrogen, protein, LDH, and potassium were noted upon statistical analysis, as follows:

Subchronic Inhalation with Endosulfan in Rats/Clinical Chemistry

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Sex Control</th>
<th>Control 0.0005mg/</th>
<th>Control 0.0010mg/</th>
<th>Control 0.0020mg/</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(air)</td>
<td>(vehicle)</td>
<td>1 air</td>
<td>1 air</td>
</tr>
<tr>
<td>One Day After End of Exposure (n=10)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>chloride (mmol/l)</td>
<td>M 101</td>
<td>103</td>
<td>103*</td>
<td>103</td>
</tr>
<tr>
<td></td>
<td>F 108</td>
<td>109</td>
<td>109</td>
<td>105*</td>
</tr>
<tr>
<td>urea nitrogen (mmol/l)</td>
<td>M 6.46</td>
<td>8.62*</td>
<td>8.11*</td>
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</tr>
<tr>
<td></td>
<td>F 7.33</td>
<td>8.29</td>
<td>7.08</td>
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</tr>
<tr>
<td>cholesterol (mmol/l)</td>
<td>M 1.83</td>
<td>1.47*</td>
<td>1.62</td>
<td>1.73</td>
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<tr>
<td></td>
<td>F 2.66</td>
<td>2.61</td>
<td>2.65</td>
<td>2.66</td>
</tr>
<tr>
<td>calcium (mmol/l)</td>
<td>F 2.66</td>
<td>2.61</td>
<td>2.65</td>
<td>2.55*</td>
</tr>
<tr>
<td>creatinine (umol/l)</td>
<td>F 48</td>
<td>52</td>
<td>49</td>
<td>51</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>58*</td>
</tr>
<tr>
<td>SGOT U/l</td>
<td>F 146</td>
<td>137</td>
<td>123</td>
<td>134</td>
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<td></td>
<td></td>
<td></td>
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<td>112*</td>
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</table>

* Statistically significant difference in parameter as compared to air-only controls at p<0.05.
Clinical Chemistry (cont'd)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Sex</th>
<th>Control 0.0005mg/</th>
<th>Control 0.0010mg/</th>
<th>Control 0.0020mg/</th>
<th>(air) (vehicle) l air</th>
<th>l air</th>
<th>l air</th>
</tr>
</thead>
<tbody>
<tr>
<td>glucose</td>
<td>M</td>
<td>8.23</td>
<td>8.22</td>
<td>11.30*</td>
<td>9.14</td>
<td>8.91</td>
<td></td>
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<tr>
<td></td>
<td>F</td>
<td>8.08</td>
<td>7.78</td>
<td>8.62</td>
<td>10.06*</td>
<td>9.26</td>
<td></td>
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<tr>
<td>mmol/l</td>
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<tr>
<td>urea nitrogen</td>
<td>M</td>
<td>7.66</td>
<td>10.50*</td>
<td>9.18</td>
<td>8.66</td>
<td>8.22</td>
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<td></td>
<td>F</td>
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<td></td>
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<td>protein</td>
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<td>59</td>
<td>55</td>
<td>53*</td>
<td>55</td>
<td>52*</td>
<td></td>
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<tr>
<td>g/l</td>
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<tr>
<td>LDH</td>
<td>M</td>
<td>69</td>
<td>48</td>
<td>92*</td>
<td>145**</td>
<td>58</td>
<td></td>
</tr>
<tr>
<td>U/l</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>potassium</td>
<td>F</td>
<td>5.2</td>
<td>5.8*</td>
<td>5.3</td>
<td>5.3</td>
<td>5.4</td>
<td></td>
</tr>
<tr>
<td>mmol/l</td>
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</table>

* Statistically significant difference in parameter as compared to air-only controls at p<0.05.
**Standard deviation = 76 (3-6 times s.d. in other groups). This value appears spurious.

The changes showing statistical significance are apparently within the biological norm for this strain and species. The increase in urea nitrogen appears more related to the vehicle than to the test substance. However, there is no conclusive evidence in this regard. The observed changes do not demonstrate significant toxicity of the test compound.

8. Macrophscopic examination of skin, orifices, eyes, teeth, oral mucosae, and internal organs followed sacrifice. The following organ weights were recorded: heart, lungs, liver, kidneys, spleen, brain, testes without epididymides/ovaries, adrenals, pituitary, thyroid, seminal vesicles. As organs were prepared for histopathological examination, macroscopic findings were noted.

Results: No dose or compound related differences between controls and dose groups were noted at macroscopic examination one day after the last administration of test substance or at examination after the recovery period. Mean absolute and relative organ weights of test groups were similar to controls at both examinations.

9. Ten males and 10 females from each group were killed one day after the last treatment. The remaining animals were killed after a 4-week recovery period. Histopathological examination of 150 rats was performed. The following organs were preserved in "fixing fluid" for microscopic examination:
heart  urinary bladder  pancreas
lungs  testes  adrenals
liver  epididymides  thymus
kidneys  prostate  pituitary
spleen  seminal vesicles  brain
stomach  ovaries  eye with optic nerve
jejunum  uterus  bone marrow (femoral)
colon  thyroid  trachea
oesophagus  ileum  salivary glands (parotid, submandibular)
duodenum  rectum  
caecum  spinal cord  diaphragm
skeletal muscle  aorta  lymph nodes (cervical, iliac)
sciatic nerve  
nose with turbinalia

Results: Several histopathological findings occurred equally in controls and in treatment groups. These were sporadic peribronchial lymphocytic aggregates and aspiration of blood in the lung; slight periportal deposition of fat in the liver; and no haemosiderin storage in the spleen. Other findings are summarized in the following table. No dose or compound related changes were produced by the test compound, according to the histopathological report.

| Subchronic Inhalation with Endosulfan in Rats/Histopathology of Organs |
|------------------|------------------|------------------|------------------|------------------|
|                  | Control (air)    | Control (vehicle) | Low (vehicle) | Mid (vehicle) | High (vehicle) |
|                  | M    | F    | M    | F    | M    | F    | M    | F    |
| Liver            |      |      |      |      |      |      |      |      |
| a) light color   | 1    | 3    | 2    |      |      |      |      |      |
| b) surface       |      |      |      |      |      |      |      |      |
| milky            |      |      |      |      |      |      |      |      |
| Testes           |      |      |      |      |      |      |      |      |
| small            |      |      |      |      |      |      |      |      |
| Kidney           |      |      |      |      |      |      |      |      |
| a) renal         |      |      |      |      |      |      |      |      |
| pelvis           |      |      |      |      |      |      |      |      |
| dilated          | 1    | 2    | 1    | 1    | 1    |      |      |      |
| b) hydro-         |      |      |      |      |      |      |      |      |
| nephrosis        |      |      |      |      |      |      |      |      |
| Spleen           |      |      |      |      |      |      |      |      |
| light color      | 1    |      |      |      |      |      |      |      |
| Ovary            |      |      |      |      |      |      |      |      |
| enlarged         |      |      |      |      |      |      | 1(R) |      |

(R)=recovery findings

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